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bugs on bugs

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fungal farmers of the insect world
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shedding light on *photorhabdus*
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Cover image Macrophotograph of the head of a worker honey bee (*Apis mellifera*). *Dr Jeremy Burgess / Science Photo Library*

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New SGM Prize Medal

Stanley B. Prusiner accepts award for 2009

SGM is pleased to announce that **Dr Stanley B. Prusiner**, Director of the Institute for Neurodegenerative Diseases at University of California, San Francisco, has accepted the invitation to be the first recipient of the Society's new Prize Medal. Amongst many awards, Dr Prusiner won the Nobel Prize in Physiology or Medicine in 1997 for his work proposing an explanation for the cause of BSE ('mad cow disease') and its human equivalent, CJD. He coined the term prion, which comes from 'proteinaceous infectious particle that lacks nucleic acid' to refer to a previously undescribed form of infection due to protein misfolding.

Dr Prusiner will deliver his Prize Lecture entitled *Prion Biology and Disease* on 1 April 2009 at the SGM Spring Conference at Harrogate (www.sgmharrogate2009.org.uk). A special symposium on prion research will also take place on the same day.

Back content of *IJSEM* goes online

The whole back content of the journal, which started out as the *International Bulletin of Bacteriological Nomenclature and Taxonomy* in January 1951, becoming *International Journal of Systematic Bacteriology* in 1966 before being retitled *International Journal of Systematic and Evolutionary Microbiology* in 2000, is now available on the HighWire site. This is a significant event in the history of microbial classification. It will greatly benefit the scientific community to have this archive freely available worldwide without a journal subscription (current access controls will remain for content that is less than 2 years old). Papers will be available in fully searchable PDF format. The archive will include hundreds of species descriptions and many seminal articles in prokaryotic systematics and taxonomy that have never been available online before in full text. *IJSEM* is the official journal of record for novel prokaryotic taxa and is published by the SGM on behalf of the International Committee on Systematics of Prokaryotes.

The back content of *Journal of General Virology* is already online and that of *Microbiology* and *Journal of Medical Microbiology* will be available soon.

Surveys on Open Access Journals

I represent SGM on the Biosciences Federation (BSF) Journals Committee. We have recently carried out surveys of BSF learned societies with journal publishing interests, and of society members as authors and readers, to find out some of the wider implications of the open access (OA) movement, and the state of awareness about the issues. This stems from the desire of some research funders, such as the Wellcome Trust and Research Councils UK, that papers from work they have funded should be made freely available online at or shortly after the time of publication. The concern of publishers is that an increase in the proportion of articles with OA could lead to a loss of subscription income. Research funders have varied in their willingness to provide money for author-side payments for OA, to replace this possible loss of subscription income. There appears also to be confusion about what mechanisms different funders have set up to provide OA funds.

The first survey indicated that publishing societies earn surpluses on their journal sales, which they recycle to support student grants, educational activities, advocacy and public awareness, and subsidized conferences. Publishing scientific journals is of course a global business: on average, around 90% of our institutional sales are 'exports'. However, to take a UK perspective, the 14 publishing societies in the survey received a total of £1,790k p.a. in subscription and other journal income from UK universities, but returned a total of £3,864k in direct support (grants, bursaries, conferences) and a further £2,299k in indirect support (educational and other charitable activities). If grossed up for all UK publishing learned societies, this clearly would amount to a very substantial amount of support for our education system and the students involved. It would be an unfortunate example of the Law of Unintended Consequences if this support was threatened by funders' OA mandates which were not matched by appropriate funding.

In the second survey, it was clear that authors and readers were much more in favour of OA through journals' own online sites or established bodies such as PubMed, than they were of 'self-archiving' on personal or departmental web pages, or institutional repositories. However, it was also clear that many authors and readers were confused about what the different types of OA and self-archiving were, and about the difference between OA and online (subscription-controlled) journals.

The BSF press release about the Committee's report is available at **www.bsf.ac.uk/journals/BSF_OA_press_release_Final.pdf** and the text of the full report is at **www.bsf.ac.uk/journals/BSF_survey_report_July_2008_FINAL.pdf**. The Committee has also prepared a guide for authors about background issues and UK funders' policies, which is at **www.bsf.ac.uk/journals/journals_authors'guide.htm**

***Ron Fraser**, SGM Chief Executive*

Nobel Prize in Physiology or Medicine 2008

This year's Nobel Prize rewards the discoveries of two viruses causing severe human diseases. One half will go to **Harald zur Hausen** (German Cancer Research Centre, Heidelberg, Germany) for his discovery of human papilloma viruses causing cervical cancer. The other half will be shared between **Françoise Barré-Sinoussi** (Institut Pasteur, Paris, France) and **Luc Montagnier** (World Foundation for AIDS Research and Prevention, Paris, France) for their discovery of human immunodeficiency virus. See the article by Robin Weiss on p. 192.

2008 Address Book

A copy of the latest edition of the Society's Address Book, giving contact details of members, should have been enclosed with your mailing of this magazine. If you did not receive one, please get in touch with the Membership Office (members@sgm.ac.uk).

Council – new structure

A Special Resolution to amend the Society's Articles of Association was passed at the AGM on 9 September 2008. This will enable implementation of the changes to the SGM's governing Council that were described on p. 106 of the August issue of *Microbiology Today*. With effect from the AGM to be held in 2009, Council will consist of six Officers and the number of Ordinary Members will be reduced to six over the period from then to September 2011. Much of the business will be transacted by subcommittees. The new Articles are available on the website at **www.sgm.ac.uk/about/articles.pdf**

Council – July meeting highlights

The SGM Prize Medal

Council devoted a significant amount of time to careful consideration of nominations for the new SGM Prize Medal to be awarded in 2009. It was agreed that the President should approach **Dr Stanley Prusiner** and he has been pleased to accept (see p. 159). A more detailed appreciation of Dr Prusiner's work will be published in a future issue of *Microbiology Today*.

Honorary Membership

Council has bestowed Honorary Membership of the Society on **Dr Volker ter Meulen**, Professor Emeritus for Virology and Immunology, Universität Würzburg, and President of the 'Leopoldina', Gesellschaft für Naturforscher und Ärzte, Sachsen-Anhalt, in recognition of his outstanding contributions to the molecular biology of paramyxo- and coronaviruses and chronic virus–host relationships, as well as for his engagement in SGM activities, science management and international microbiology promotion.

Professor Sir Howard Dalton

Council was pleased to hear that SGM had been remembered in the will of former President, the late **Professor Sir Howard Dalton FRS**. The bequest of £2,000 will be used to promote microbiological projects in The Gambia where Sir Howard and his wife Kira carried out charitable work.

SGM finances

Council approved the membership fees and SGM journal subscription prices for 2009. These will increase by on average 4%.

Laboratory-based microbiology projects for medically qualified graduates

The Treasurer announced that there will be a new grant scheme to support medically qualified graduates taking up a career in medical microbiology. The grants will fund the consumables part of short-term research projects in a 'home' hospital or another host laboratory. Applications to the scheme are invited for 2009; see **www.sgm.ac.uk/grants**

Retiring members of Council

The President thanked the retiring member of Council, **Professor Bert Rima**, Queen's University, Belfast, for his highly appreciated input to the activities of Council. He also noted the significant contributions of **Professors Iain Hagan** and **Rick Randall**, who had resigned from Council earlier in the year, before the end of their terms of office.

***Ulrich Desselberger**, General Secretary*

SGM Staff

Congratulations to **Stefan Sidorowicz** and his wife Helen on the birth of a baby daughter Laura in July, and to **Nicolas Fanget** and his wife Amina on the birth of a baby son Bilal in October.

Farewell to **Gemma Sims** who worked here for a year to develop a microbiology teaching resource to meet the requirements of the new A levels. This should be ready for distribution to UK schools early in 2009. We wish Gemma well in her new post as teacher of biology at Leighton Park School in Reading.

New elected members of Council

The following will serve on Council for 4 years from 9 September 2008:

Professor Mark Harris

I graduated with a first class honours degree in Biological Sciences from Plymouth Polytechnic in 1983 and then undertook my PhD at the Institute of Virology in Glasgow, working with Ron Hay on adenovirus DNA replication. After a postdoc at the NERC Institute of Virology in Oxford working on baculoviruses with Bob Possee, I moved back to Glasgow to the Department of Veterinary Pathology, switched from DNA to RNA viruses, and began working on the Nef protein of HIV-1 in the lab of Jim Neil. After 5 years as a postdoc I obtained an MRC Senior AIDS Research Fellowship and subsequently moved to Leeds in 1997, taking up a Lectureship post in what was then the Department of Microbiology. Whilst retaining an interest in HIV, my lab has moved over almost entirely to the study of hepatitis C virus. My research is focussed both on basic mechanisms of virus replication as well as virus–host protein interactions. Our funding comes from a variety of sources including research councils, the Wellcome Trust and industry. I have always been a strong supporter of the Society – I am currently an Editor of *Journal of General Virology* and serve on the Virus Division committee. I welcome the opportunity to make a further contribution to SGM activities as a member of Council.

Dr Gary Rowley

Gary Rowley is a lecturer of bacterial pathogenesis within the School of Biological Sciences, University of East Anglia. He did his PhD with Professor Mark Roberts, University of Glasgow, and then moved to the Institute of Food Research, as a postdoc in Professor Jay Hinton's Laboratory. He moved to UEA in 2007 to take up a Faculty position. His research interests focus on the environmental regulation of bacterial virulence genes using the intracellular pathogen *Salmonella* Typhimurium as a model organism. Recent work has focused on investigating the role of the envelope stress response in pathogenesis and the mechanisms that *Salmonella* uses to detoxify nitric oxide.

Congratulations to …

SGM Education Officer **Dr Sue Assinder** on her appointment as Director of Education, Liverpool School of Tropical Medicine.

Professor David Baulcombe (University of Cambridge) on winning the 2008 Albert Lasker Basic Medical Research Award. Along with Victor Ambros and Gary Ruvkun, the award honours the scientists who revealed an unanticipated world of tiny RNAs that regulate gene activity in plants and animals. Baulcombe made his discovery whilst probing how plants defend themselves against viruses.

Professor Nigel L. Brown, former Director of Science and Technology at the BBSRC who has moved to the University of Edinburgh as Vice-Principal and Head of the College of Science and Engineering.

Professor Iain Hunter (University of Strathclyde) on his new post as Dean of the University's Faculty of Science. Professor Hunter has been Professor of Molecular Microbiology for the past 13 years.

Professor Richard James (Head of the School of Molecular Medical Sciences, University of Nottingham) on being awarded the SfAM Communications Award 2008 for raising the profile of his applied microbiology work to the public.

Douglas Kell, Professor of Bioanalytical Science, University of Manchester, who is to be the new Chief Executive of the Biotechnology and Biological Sciences Research Council. He is a leading figure in the world of systems biology.

Professor Hilary Lappin-Scott (University of Exeter and SGM Scientific Meetings Officer) who will be taking up a new post at Bangor University in January 2009 as Pro Vice Chancellor for Research.

Deaths

The Society notes with regret the deaths of:

Professor Peter Gilbert (University of Manchester), a distinguished expert on biofilms and a member since 1974. Professor Gilbert was due to speak at the recent SGM meeting in Dublin and the programme was changed so that Professor Michael Brown could deliver a tribute. A reception was also held to honour Peter's memory.

Professor Christopher Thurston, a member since 1972, died in August after a long illness. A full obituary appears on p. 210.

Grants

NEW! – Medical Trainee Support Grants

Funding for medical microbiology trainees (during foundation or specialist training) to carry out short lab-based projects on a microbiological topic. The grant covers a contribution towards consumables costs only. Closing dates: **20 March** and **25 September 2009**.

Student Schemes

GRADSchool Grants

Postgraduate Student Associate Members registered for a PhD in a UK university can apply for funding to support the full cost of course fees for a GRADschool. Students funded by Wellcome Trust, BBSRC, NERC, MRC or EPSRC are entitled to a free place on a GRADSchool course and should not apply to this scheme. Applications, on the appropriate form, are considered throughout the year but must be made before booking a place on a course.

Student Meetings Grants

Grants contribute towards travel, registration and accommodation expenses for attendance at one SGM meeting each year. Applicants must be Postgraduate Student Associate Members resident and registered for a PhD in an EU country or Undergraduate Members based at a university in the UK or Ireland accepted to present work the meeting. Closing date for Edinburgh: **27 March 2009**.

Elective Grants

Funding for medical/dental/veterinary students to work on microbiological projects in their elective periods. Closing dates: **20 March** and **25 September 2009**.

Vacation Studentships

The 2009 scheme is now open for applications. As described on p. 208, the scheme offers a great opportunity for undergraduates to work on microbiological research projects during the summer vacation before their final year. The awards, which are made by competition, aim to give students experience of research and to encourage them to consider a career in this area. The studentships provide support at a rate of £185 per week for a period of up to 8 weeks. An additional sum of up to £400 for specific research costs may also awarded. Applications must be from SGM members on behalf of named students.

The closing date for applications is **13 February 2009**.

Student Society Sponsored Lectures

These cover the travel and other expenses of up to two speakers on microbiological topics per Society each year at student society meetings.

Scientific Meetings Travel Grants

This scheme is open to a range of early-career microbiologists resident within the EU, ranging from postgraduate students through to first postdocs and newly appointed lecturers. Funding is tiered according to the location of the meeting. The maximum grants are: UK (or country of residence) – **£200**; within Europe – **£350**; Rest of World – **£500**. These grants may also be used to support attendance on short courses.

President's Fund for Research Visits

Grants are available to support short research visits (1–3 months) by early-career microbiologists resident within the EU, ranging from postgraduate students through to first postdocs and newly appointed lecturers. Funding is limited to a maximum of **£3,000**. Retrospective applications will not be accepted. Closing dates: **20 March** and **25 September 2009**.

Public Understanding of Science Awards

Are you planning any projects to promote the public understanding of microbiology? Have you got a National Science Week event in mind? SGM can help. Grants of up to **£1,000** are available to fund appropriate activities. Applications are considered on a first come, first served basis throughout the calendar year.

SGM has a wide range of grant schemes to support microbiology. See **www.sgm.ac.uk/grants** for details and closing dates.

Enquiries should be made to the Grants Office, SGM, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (t 0118 988 1821; f 0118 988 5656; e grants@sgm.ac.uk).

Lister Institute Research Prizes 2009

Applications are now invited from young clinicians and biomedical scientists for the *2009 Lister Research Prizes*. The Prizes offer £200,000 to be spent on the recipient's research in whatever way they choose, other than for personal salary, and therefore provide unfettered research funding. Prizes will be allocated on the basis of the applicant's research proposal and track record. Applications may be in any area of biomedical science or related areas. Further information and forms are available from the Lister's website (www.lister-institute.org.uk) or directly from the Institute's Administrator (secretary@lister-institute.org.uk). Closing date: **5 December 2008**.

Centre for Bioscience – The Higher Education Academy

National Teaching Fellows

Individual awards for 2008 have been made to two SGM members, **Dr Annette Cashmore** (University of Leicester) and **Dr Julian Park** (University of Reading). The awards recognize and celebrate individuals who make a significant impact on the student learning experience.

Report on first-year undergraduate practicals

This report is the outcome of a workshop held in April 2008 by the Centre to discuss first-year undergraduate work in the biosciences. Participants shared experiences of delivering practical classes where problem-solving, research investigation, creativity and innovation are key features. Amongst several disciplines, the report describes five microbiology investigations which can be downloaded from the Centre website (www.bioscience.heacademy.ac.uk/events/themes/1styrpracticals.aspx).

SGM membership subscriptions 2009

The following rates were agreed at the AGM of the Society on 9 September 2008.

Membership category		Annual subscription		Additional subscriptions for publications (print only)							
				Microbiology		*JGV*		*IJSEM*		*JMM*	
		£	US$	£	US$	£	US$	£	US$	£	US$
Ordinary		54	108	106	212	106	212	106	212	60	120
Associate *Postgraduate Student Retired Microbiologist with annual salary <£26.5k*		25	50	48	96	48	96	48	96	48	96
Undergraduate		10	NA	NA	NA	NA	NA	NA	NA	NA	NA
School		10	NA	NA	NA	NA	NA	NA	NA	NA	NA
Corporate	Tier 1	350	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Tier 2	500	NA	NA	NA	NA	NA	NA	NA	NA	NA

For airmail despatch of *Microbiology Today*, add £19/US$36 to subscription.

Members are reminded that their 2009 subscriptions are due for payment by **1 December 2008**.

As in previous years, no journal or meetings information will be despatched to members who are in arrears, and there will be no guarantee of provision of back numbers of journals for members who pay their subscription late.

Payment against invoice

Invoices were despatched recently to all members who pay by this method. If you did not receive one, please inform the Membership Office.

New secure online credit card renewal payment

If you pay against invoice, you can renew your subscription online via the SGM website (www.sgm.ac.uk/members) with either a credit or debit card. Please see your invoice for details.

Payment by direct debit

Subscription notices were despatched recently to all members paying by direct debit. To continue your present status and journal requirements, no further action is necessary. To change your membership status or journal requirements for 2008, you should have amended your subscription notice and returned it to the membership office by **10 November 2008**. However if you have missed this deadline, your amended notice will be accepted if it is submitted immediately.

Please note

Continuous credit card payments are no longer available. Alternative methods are by direct debit (for UK bank account holders) or one-off credit/debit payment online.

Income tax relief on membership subscriptions

Members who are liable for UK income tax are reminded that their annual subscriptions to the Society have been approved by the Inland Revenue as qualifying for income tax relief. Any member who would like further information or has difficulty in obtaining this relief should contact the Chief Executive (r.fraser@sgm.ac.uk).

microshorts

Lucy Goodchild takes a look at some stories that have hit the headlines recently.

▲ Cotton bollworm caterpillar. *Nigel Cattlin / SPL*

► Biting midge (*Culicoides* sp.) feeding on human blood. *Sinclair Stammers / SPL*

GM cotton reduces pest damage

A 10-year study by scientists at the Chinese Academy of Agricultural Sciences in Beijing has revealed that the benefits of genetically modified cotton extend further than had previously been anticipated. Cotton modified with a gene from *Bacillus thuringiensis* to make its own insecticide was able to resist attack from its biggest pest, the cotton bollworm. The study, published in *Science*, showed that the GM crop resulted in a '*dramatic long-term decline*' in damage. The pest-resistant crop even reduced the cotton bollworm population in neighbouring fields, a surprising result for the researchers.

www.timesonline.co.uk/tol/news/uk/science/article4783078.ece

Scientists discover 'virophage'

Scientists have discovered a virus that can be infected by another virus, according to research published in *Nature*. The giant virus, called mamavirus, infects amoebae. When researchers from the Université de la Méditerranée in Marseille, France, studied the virus using an electron microscope, they discovered an associated virus, which they called Sputnik. This smaller virus is incapable of infecting cells on its own. As it has only 21 genes, Sputnik hijacks mamavirus machinery in order to infect cells, so it has been dubbed a 'virophage'. By hijacking it, Sputnik reduces the infectivity of mamavirus. Giant viruses are able to infect climatically important plankton, which produce dimethylsulfide. Therefore, by reducing the infectivity of mamavirus, Sputnik virus could potentially affect climate change.

www.nature.com/news/2008/080806/full/454677a.html

Bar-coding midges to stop spread of bluetongue

Scientists have developed a method of genetically 'bar-coding' biting midges that could help prevent the spread of bluetongue disease. Researchers from the University of Aberdeen collected 1 million midges in 37 light traps in Scotland between late 2007 and early 2008. They used a pioneering DNA test to identify the midges *Culicoides obsoletus*, *C. chiopterus*, *C. dewulfi* and *C. scoticus,* and create a map of their geographical distribution in Scotland. In southern Europe, *Culicoides imicola* carries various strains of bluetongue virus and is responsible for its spread across the continent. However, the virus has been found in different midge species in the UK and scientists are tracking them to gauge the speed at which the virus might spread if it reaches Scotland. The study revealed that midge numbers were dependent on climatic and geographic conditions.

www.alphagalileo.org/index.cfm?fuseaction=readrelease&releaseid=531840

Vaccines for bacteria

Bacteria used in industrial processes could be protected from virus infections using a kind of vaccine, according to research published in *Science*. German researchers at Wageningen University uncovered the mechanism some bacteria use to defend themselves in the long term against potentially lethal viruses: this has potential to protect good bacteria and target pathogenic species. Bacteria insert pieces of viral DNA into their own genome. The 'adopted' segment is used like a snapshot to help the bacterium remember the virus and kill it during a subsequent infection. The researchers identified six bacterial proteins involved in the defence system; one cuts the 'adopted' segment out of the bacterial genome and helps the other five proteins to compare it to the DNA of the invading virus. This mechanism could be utilized to protect industrially important bacteria from being attacked by bacteriophages. It could also be targeted to combat antibiotic-resistant bacteria; by deactivating the system, bacteria would be left defenceless and susceptible to bacteriophage attack.

www.alphagalileo.org/index.cfm?fuseaction=readrelease&releaseid=531517

▲ Two variants of the Harlequin ladybird. *Sheila Terry / Science Photo Library*

Ecologists find invasive ladybird's Achilles' heel

The Harlequin ladybird was introduced to the UK 4 years ago as a form of biological control of aphids and it has since become an invasive species, posing a major threat to native ladybirds. The Harlequin is larger and more aggressive than native ladybirds and is also resistant to a deadly fungus, *Beauveria bassiana*, that threatens native species. Although Harlequin ladybirds do not succumb to infection with the fungus, the number of eggs they lay after exposure to the pathogen is dramatically reduced. However, because the fungus is so deadly to the already endangered native ladybirds, it is not a viable means of controlling the invaders. Speaking at the British Ecological Society's conference at Imperial College London, scientists say they are now looking at semiochemicals, which the insects use for communication, to control Harlequin ladybirds.

www.alphagalileo.org/index.cfm?fuseaction=readrelease&releaseid=531792

Mosquitoes lured by odourless chemical

Catching mosquitoes is a key part of the surveillance of vector-borne diseases like West Nile virus, encephalitis and lymphatic filariasis. People who monitor the mosquito traps, and even those who live near them, have to suffer the highly offensive smell of the attractants currently in use. Now, scientists at the University of California, Davis in the USA have developed a low-cost attractant that lures mosquitoes without making humans hold their noses; it is odourless to us, but enticing to mosquitoes. The synthetic mixture contains trimethylamine and nonanal in low doses and extensive field research in Brazil showed it is as effective as the lure currently used. Gravid female traps target mosquitoes that have fed on blood and are ready to lay eggs. Because mosquitoes lay hundreds of eggs at a time, catching females ready to lay can reduce the number of mosquitoes capable of spreading diseases dramatically. The research could play a key role in surveillance and control programmes for *Culex* mosquitoes.

www.newspostonline.com/sci-tech/killing-mosquitoes-without-raising-a-stink-just-became-a-reality-200808313789

Historical research highlights

The entire back-catalogue of *IJSEM* is now online – here's a snippet from the content.

2005: Scientists identify olive fly symbiont after 96-year search

In 1909, Petri described an example of hereditary symbiosis in the olive fly after observing unidentified bacteria under a microscope. He suggested that the symbiont might be *Bacterium* (*Pseudomonas*) *savastanoi*, which causes olive knot disease, as it could be isolated from the larvae. Petri postulated that the bacterium might be unculturable, a speculation that has remained the case for almost a century. In 1965, Buchner analysed the bacterium, followed closely by Hagen in 1966, but neither disputed Petri's designation.

In 2005 Capuzzo *et al.* from Università di Padova and Università di Udine in Italy proposed the novel species '*Candidatus* Erwinia dacicola'. By sequencing the entire 16S rRNA gene, they were able to show marked similarity with enterobacterial lineages, with close matches to *Erwinia persicina* and *Erwinia rhapontici*.

Adults of the olive fly *Bactrocera oleae*, the most important pest of olive trees, carry the bacteria in an organ called the oesophageal bulb. The bacteria replicate rapidly and form masses that reach the midgut. The mother transmits the bacteria to her eggs during oviposition, then the bacteria multiply inside the larvae. By rearing the flies on artificial media, the scientists observed that the progressive loss of the symbiotic bacteria resulted in lower vitality and fertility of the flies. Furthermore, flies lacking the symbionts were more prone to infection by other microbial species.

Although the evidence suggests a symbiotic relationship between the bacteria and the olive fly, the bacteria still could not be cultured. However, the availability of modern DNA-based methodologies allowed the researchers to succeed where Petri had not: to clarify the systematic placement of the microbes and to trace their connections to related species.

IJSEM 55, 1641–1647 (doi: 10.1099/ijs.0.63653-0)

Microbial diseases of bees

Bees come under attack from a wide range of microbes. **Travis R. Glare** and **Maureen O'Callaghan** consider the role of bee diseases in the worldwide decline of these key ecosystem providers.

The humble bee has a special place in our lives. Essential for pollination of many plants, including food crops, the provider of honey and royal jelly and many other products, bees are important to the economies of countries and, as ecosystem service providers, have few equals among insects. There is a quote, often attributed to Einstein, suggesting that if all the bees disappeared then humans would follow within 4 years. While this is perhaps an overstatement, a recent estimate of the contribution of insect pollination, mainly by bees, to agriculture was €153 bn.

There are many threats to bee survival, including the risk of disease caused by micro-organisms. The vast majority of our knowledge of bee diseases focuses on the honey bee, *Apis mellifera,* although there are actually over 20,000 species, both stingless and stinging, from those with solitary lifestyles to complex societies such as honey bee hives.

Viruses, fungi, protozoa and bacteria are all known to cause infections in bees, sometimes leading to collapse of colonies, and causing serious threats to the bee-keeping industry. Bees have two distinct life forms, brood (egg, larva and pupal stages which develop within the hive) and adult. Most diseases are specific to just one of these life stages. While the list of diseases is quite long, only a few are of serious concern to apiculturists.

Major disease of bees

Various evocative names, based on the visual symptoms of diseased bees, are used to describe the most problematic diseases, for example foulbrood, sacbrood and chalkbrood.

American foulbrood (AFB) is caused by the spore-forming bacterium *Paenibacillus larvae*. The disease was first described in 1769. AFB is probably the most virulent disease of honey bee brood and is capable of causing the collapse of bee colonies. The name describes the symptoms of diseased brood; infected cells become discoloured, sunken and there is a characteristic smell. Adult bees are not affected. This disease has traditionally been treated with the antibiotic oxytetracycline, but some bacterial strains have developed resistance to this and the disease is now increasing in prevalence around the world. Although the disease was first described over 200 years ago, much is still unknown about this infection. A German research team has only recently discovered how the bacteria kill larvae, by building up to very high numbers in the gut before bursting into the haemocoel, causing death.

European foulbrood (EFB) is caused by the non-spore-forming bacterium *Melissococcus* (=*Streptococcus*) *plutonius*. Unlike AFB, EFB usually affects unsealed brood, and the recently dead larvae present as watery and yellowish brown cadavers twisted inside the cell. Despite the importance of EFB, the disease is poorly understood, but like AFB, has increased in prevalence in recent years.

Of the fungi known to infect bees, species of the fungus *Ascosphaera* are the most common. *Ascosphaera apis* is the causative agent of the well known chalkbrood disease in honey bees, so called because of the chalky appearance of infected brood. Chalkbrood is usually considered a minor disease of bees, as is stonebrood, caused by the fungus *Aspergillus*.

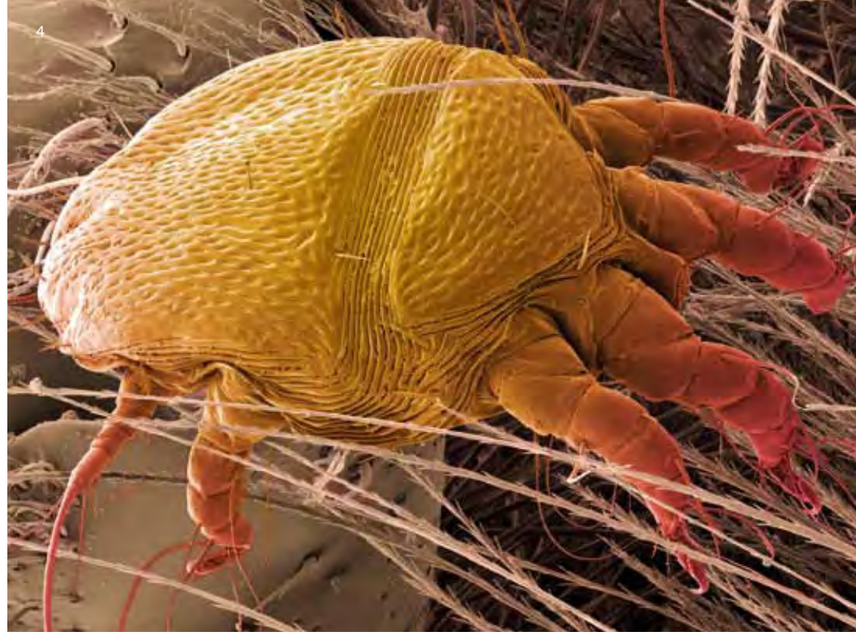
Viruses can also cause devastation in bee colonies. At least 18 types of viruses have been found infecting honey bees alone. Going by some delightfully descriptive names (e.g. deformed wing virus, chronic paralysis virus, acute bee paralysis, sacbrood virus and black queen cell virus), these viruses range from non-lethal to causing significant mortality in nests. One of the more interesting aspects of viral disease is that many infections cause no obvious symptoms much of

▲ 1. Sunken brood capping with holes suggests American foulbrood (AFB). *Zachary Huang, Michigan State University, USA*

2. A dead larva killed by AFB usually forms a 'false tougue' pointing upward. *M.V. Smith, University of Guelph, Canada*

3. Larvae showing typical European foulbrood (EFB) symptoms. These larvae show yellow streaks. *M.V. Smith, University of Guelph, Canada*

◀ A honey bee (*Apis mellifera*) feeding. *Dr John Brackenbury / Science Photo Library*



▲ 1. Chalkbrood, whereby the larvae become mouldy with white hyphae, then hardened to be similar to pieces of white chalk. This disease is mostly considered a stress disease, only occuring in weak, or in otherwise stressed colonies. *M.V. Smith, University of Guelph, Canada*

▲ 2. Close-up of the head of a larva killed by Sacbrood. *M.V. Smith, University of Guelph, Canada*

► 3. A honey bee (*Apis mellifera*) with two *Varroa jacobsoni* mites on its thorax. *Maryann Frazier / Science Photo Library*

► 4. Coloured SEM of a *Varroa* sp. honey bee mite. *Steve Gschmeissner / Science Photo Library*

the time. Kashmir bee virus can persist in bee populations causing no obvious symptoms, only to explode into lethal infections, possibly triggered by bee stress factors such as attack by the *Varroa* mite. *Varroa* mites are parasites on honey bees and have spread around most of the world, causing significant losses in hives as well acting as vectors for some viruses. Virus infections can be hard to detect and diagnose, as symptoms, if any, resemble other mortality causes.

Emerging diseases

Microbes are constantly evolving, leading to the emergence of new strains with novel pathogenic abilities. For example, some honey bee diseases appear to have widened their host range in recent years. Protozoa of the genus *Nosema* infect many invertebrates, and individual species are typically quite limited in their host range. *Nosema apis* has long been recognized as causing one of the most important diseases in adult honey bees, infecting the guts of adult bees. However, *Nosema ceranae*, thought to infect only the Asiatic or Eastern honey bee, *Apis cerana*, has recently been shown to infect the European honey bee, *A. mellifera*. Evidence is emerging of recent spread of *N. ceranae* in honey bee populations around the world since around 1998. There is ongoing risk that other highly virulent diseases of honey bees will emerge.

Bees under stress

There is still so much we don't know about how combinations of microbial diseases, parasites, pollution and urbanization are affecting bees. Colony Collapse Disorder (CCD) is the name given to the recent widespread mortality of worker (adult) honey bees on several continents, especially North America. The sometimes startlingly high mortality rates have not been attributed to a particular cause. Several recent studies suggest that some colony collapse is caused by a combination of disease and the parasitic attentions of *Varroa* mites. Various studies have found that prevalence of viral and protozoan diseases is higher in *Varroa*-infected hives and *Varroa* is thought to be capable of acting as a vector for pathogenic microbes. In some cases, viral diseases that do not usually cause high mortality are rampant in hives with *Varroa* or have been associated with CCD. Israeli Acute Paralysis Virus (IAPV) was recently found to be the most consistent indicator of CCD, as well as Kashmir bee virus and *Nosema* spp. However, no causal link has been made between IAPV and CCD. As with all living things, stress increases the susceptibility of the host to a pathogen, and if bees are under stress, disease can be more debilitating. Whether CCD is only caused by the interaction between a specific stress such as *Varroa* and some diseases, or widespread interaction between a number of stresses is unclear. Combinations of stresses could include multiple diseases. Using molecular techniques, several studies have shown multiple diseases infecting single bees. So diseases, some of which may not normally cause death, could act together to kill. Additionally, nutritional stress can exacerbate the incidence of pathogens.

How do diseases spread?

How diseases spread between individuals is still largely unknown. Both horizontal transmission (where viruses are transmitted among individuals of the same generation), and vertical transmission (where the disease is passed from queens to their offspring) are known. Modern molecular-based techniques have contributed significantly to our understanding, allowing investigation of whether pathogens are present inside eggs, and by establishing the relatedness of occurrences of disease in different hives. It is obvious how some diseases spread; the presence of large numbers of spores, whether fungal, bacterial or protozoan, inside a hive will contaminate brood and/or workers that come in contact. However, some more unusual routes have also been demonstrated. DNA from viral pathogens has been detected in the semen of honey bee drones, suggesting that mating may spread some disease both horizontally and vertically. Pathogens can be transmitted in bees and sometimes in bee products, prompting many countries to closely regulate the importation of bees and honey.

How do bees defend themselves from disease?

The high density populations and conditions within the bee colony (enclosed, moist, dark, poorly ventilated) are ideal for the outbreak and spread of disease. Fortunately, because bees are constantly exposed to pathogenic micro-organisms, they have evolved strategies to resist infection. The cuticle of bees acts as a barrier to penetration, and immune system-based defence can prevent infection of many minor pathogens. However, the recent completion of the honey bee genome sequence has shown that they have only about a third of the number of known immunologically related genes when compared to flies or mosquitoes, suggesting that bees rely less on individual immunity than most insects.

Bees, in common with a number of other social insects, have well developed behavioural responses to combat disease. These behavioural responses are collectively known as hygienic behaviour and include recognition and removal of diseased brood by worker bees. Bee species, and even different hives of the same species, differ in their ability to perform hygienic behaviours, with some colonies far superior to others. Some strains of bees are capable of recognizing diseased brood well before it is a threat to the hive, and remove diseased individuals. In some cases, the task of disposing of diseased insects falls to specialist 'undertaker bees' that appear to be old workers. Bees are also assisted in resisting disease by propolis, present in the plant resins collected by honey bees and used as a sealant in the hives. Propolis is known for its antimicrobial properties.

What hope is there for the future?

With increasing prevalence of disease, unexplained disappearance of bees on some continents and the emergence of new diseases, bee populations are under threat. Fortunately, increasing sophistication of research methods is allowing unprecedented understanding and insights into bee pathology by allowing detection of cryptic infections, generation of epidemiological data and detailed understanding of bee–pathogen interaction. With increasing understanding comes a better appreciation of the role of disease and methods for reducing impact. For example, the presence of Kashmir bee virus has been detected in the UK, despite never being identified as a cause of infection in UK bees based on visual symptoms. This suggests a potential non-lethal role for this virus. Detection of virus associated with CCD may also lead to a cure. Separating the various factors affecting bee colonies will allow the causal agents to be directly treated. Without understanding of the cause of CCD, no cure will be possible, but when the factors are known, many large and small mitigations can be used.

The risk is that with increasing pressure from civilization, bees could suffer increasingly from threats and stress, including increasing prevalence of disease. A better understanding of bee dynamics and the development of mitigations is urgently required.

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Ancient fungal farmers of the insect world

Not only humans practise agriculture. As **Garret Suen** and **Cameron R. Currie** describe, ants have amazing systems of growing fungal crops in their 'gardens' too.

◀ A worker of the leaf-cutting ant *Acromyrmex octospinosus* tends to her fungus garden. These ants grow bacteria on their body and use the antibiotics the bacteria produce to protect their gardens against infection from invading pathogens. *Heidi Horn*

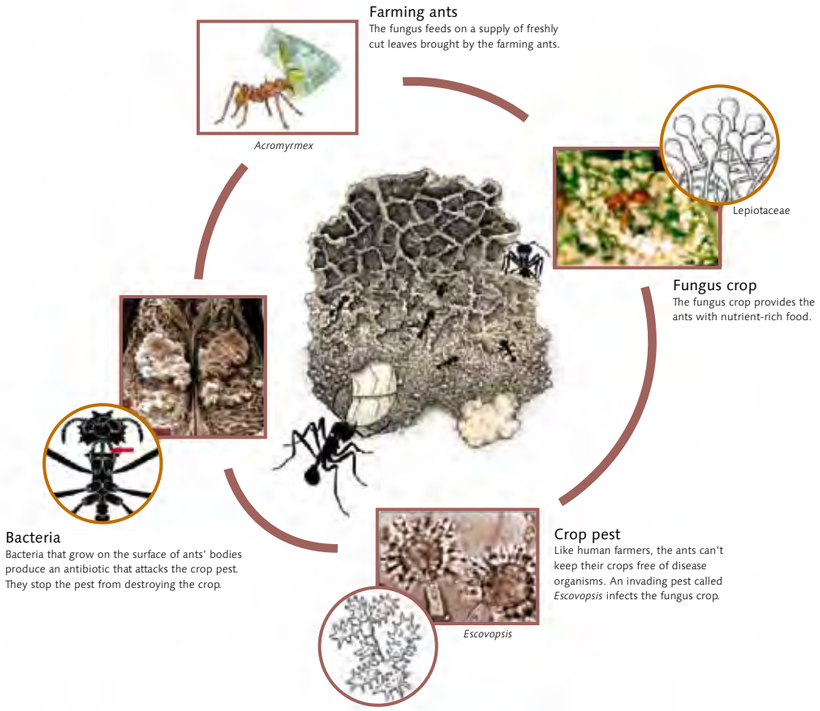
Take a stroll through a rain forest in South America and you might find yourself walking in a river, not of water, but of leaves. Leaf-cutter ants swarm in the underbrush, carrying their precious cargo back to their nest with an apparent single-minded determination. This conspicuous behaviour has made these ants one of the most dominant herbivores in the Neotropics, and one of the most successful social insects in nature. A closer look at the ants reveals that they are ancient farmers, having developed the secret of agriculture over 50 million years ago. Using their freshly-cut leaves, they incorporate them into gardens where they grow a specialized fungus that they consume for food. This relationship between ant and fungus has been described as a breakthrough in animal behaviour, and parallels the practice of sustainable agriculture in humans, arguably the most important development in human civilization that, in our opinion, resulted in the dominance of humans on planet Earth.

Leaf-cutting ants are the most highly-derived group of ants that practice fungus growing. A total of four other fungus-growing ant agricultural systems have been described, spanning over 200 different species of ants, each based on the type of fungus grown and the material incorporated into their gardens. The vast majority of fungus-growing ants do not cut leaves, but instead collect fruit, leaf litter and decomposing organic material, such as caterpillar dung, to grow their fungus.

Fungus-growers also have diverse colony sizes, with some species containing only a few hundred workers, while many leaf-cutting ant species can contain upwards of 5 million. All species, however, follow the same life cycle. Organic material is brought into the colony by foragers and is then processed to form a garden matrix where the fungus grows. New material is continuously incorporated into the gardens in order to propagate the fungus, and old material is removed by the ants and placed in special refuse dumps away from the colony. In many groups of fungus-growing ants, the fungus produces specialized packets of nutrients called gongylidia that the ants eat and feed to their developing brood. At the start of the rainy season, the colony produces male and female winged reproductives called aletes, which mate in a spectacular display of flying ants. The newly-mated queens then go on to found new colonies. Young queens transport a small piece of the fungus garden in a special organ known as an infrabuccal pocket when they leave the nest for their mating flights, and thus ensure that they can successfully start a fungus garden in the new colony.

Garden microbiology

Until about a decade and a half ago, research on fungus-growing ants focused primarily on the ants and their foraging behaviour. It wasn't until the early 1990s that this focus shifted to the fungus gardens and their associated microbial communities. Since the ant gardens are maintained in soil chambers, they are routinely exposed to a number of potential pathogens



◀ Fig. 1. The fungus-growing ant system. The ants grow a fungus crop for food in gardens, which often get attacked by invading crop pests. The ants deal with these attacks by growing bacteria on the surface of their bodies that produce antibiotics capable of stopping the pest. *Cara Gibson & Angie Fox*

▼ Fig. 2. A fungus garden from a 1-year-old colony of *Acromyrmex echinatior*. Note that many of the garden workers are covered with the antibiotic-producing bacteria. *David R. Nash*

▶ Fig. 3. Rivers of leaves. Foragers of the leaf-cutter ant *Atta cephalotes* bring freshly-cut leaves back to their nest. *Alexander Wild*

that could infect and overtake a garden. In fact, many of the ant colonies do become overgrown by fungal pathogens, often resulting in the death of the colony. Intensive sampling of the fungal communities within the gardens revealed that a specialized microfungal pathogen selectively attacks the gardens of the fungus-growing ants. These fungi, which belong to the genus *Escovopsis*, directly attack and kill the crop fungus, and can overrun the garden in a similar fashion to the way weeds and pests can ruin human gardens.

A curious observation that researchers noted was that some workers had a white wax-like substance across their bodies. It was thought that this substance was a wax produced by the ants themselves, with an unknown function. However, when viewed under a microscope it was discovered that this covering was not a wax, but a bacterium! Isolation of these bacteria revealed that they belong to the genus *Pseudonocardia*, which are part of the actinobacteria, a group of prokaryotes that produces over 80% of the antibiotics used by humans. Further work on this ant-associated actinobacteria has shown that it produces antifungal compounds that inhibit the specialized microfungal pathogen that attacks the garden. As a result, it is now known that these ants employ these bacteria as a source of pesticides to control the invading pathogenic fungi. Interestingly, the spread of the actinobacteria on

worker ant bodies is correlated to the incidence of infection. At the onset of invasion by *Escovopsis*, the actinobacteria will cover the workers' bodies, presumably to increase the production of the pesticide. This discovery was the first demonstrated example of an animal, other than humans, that employ bacteria to produce antibiotics in order to deal with pathogens.

As a second line of defence, the ants have also adopted the practice of weeding. Anyone who has ever weeded a garden can readily identify with this onerous task! When *Escovopsis* is detected by garden workers, there is an immediate flurry of activity as ants begin to comb through the garden matrix. Upon finding the pathogenic fungus, they weed them out and discard them into their refuse dumps away from the garden. By weeding and applying pesticides, the ants have developed a system to keep their gardens pest-free, an impressive feat given that they grow their fungal crop in monoculture, an ability which has evaded human agriculturalists.

Mutualism happens

The interaction between the ants and their fungus crop, and the ants and the bacteria is known as a mutualistic relationship. In general a mutualism is established when both members of the interaction derive a benefit from the association. In the ant–fungus mutualism, the ants obtain nutrients from the fungus, and use this to feed the entire colony. This mutualism is so tight, that the loss of fungus by the ants results in the death of the entire colony. In return, the fungus receives a continuous supply of growing material, protection from the environment, and the removal of disease-causing agents and competitors through the ants' weeding behaviour and pesticide application.

So what do the bacteria get out of producing pesticides for the ants? For starters, they get food. Many species of fungus-growing ants have evolved special crypts on their bodies where the bacteria live and grow. It is thought that the ants provide nutrients to the bacteria through glands connected to these crypts. Furthermore, the bacteria gain a protected environment in which to grow, away from the intense competition they would face if they lived in other environments such as the soil. Since the ants are invested in these bacteria as a producer of pesticides, they are carried by young queens that found new nests, and thus gain access to new resources that ensure their continued existence and survival.

A chemical arms race

Research in our laboratory has revealed a number of interesting properties between the bacteria and the pathogenic fungus. The bacteria appear to be specially suited to inhibiting the pathogenic fungi that infect the ants' fungus garden. Even though these parasitic fungi belong to a single genus, they are differentiated into various species and strains that are each associated with particular groups of ants. We have found that the actinobacteria associated with any given species of fungus-growing ant is effective at inhibiting some strains of pathogenic fungi, but not all; they tend to be most effective against the pathogenic fungus that specifically infects the gardens of the ants they are associated with. Interestingly, the tight association between ant, bacteria and pathogen will sometimes result in the pathogen winning. This interplay has been described as a chemical 'arms race' between the bacteria and fungus, with one side beating the other as new compounds are evolved. At the moment, we are beginning to understand the chemical warfare at the genetic level, and it is likely that these types of interactions are more prevalent in nature than previously thought.

So how exactly does an ant go about forming partnerships with a fungus and a bacterium? No one really knows. With new advances in molecular and genetic technologies, such as whole-genome sequencing, we will hopefully begin to understand how these associations were established, and gain further insight into how these interactions resulted in the remarkable fungus-growing ability of the ants.

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Bacterial sequences in an invertebrate genome

The genomes of many nematodes and arthropods contain bacterial sequences. How did they get there? **Julie C. Dunning Hotopp** and **Jason Rasgon** explain.

▲ *Wolbachia* infect the most abundant animal phyla including nematodes and arthropods. This includes some bees and butterflies like those shown here. *J.C. Dunning Hotopp*

Wolbachia pipientis is the most prolific intracellular endosymbiont on earth. These bacteria infect not only 70% of insects, but also the most abundant animal phyla, including nematodes and arthropods.

The arthropod-infecting *Wolbachia* exert unusual effects on host reproduction, including: (1) parthenogenesis, whereby infected virgin females produce infected female offspring, (2) male killing, whereby infected male embryos fail to develop, (3) feminization, whereby genetic males develop into reproductively capable females, and (4) cytoplasmic incompatibility, the most common phenotype, whereby the offspring of uninfected females and infected males fail to develop. *Wolbachia* are maternally inherited, being transferred through the egg cytoplasm. Therefore, these reproductive phenotypes favouring *Wolbachia*-infected females increase the proliferation of *Wolbachia*-infected arthropods. *Wolbachia* are parasitic endosymbionts, since the interaction benefits *Wolbachia* while exerting a negative effect on the host by limiting genetic exchange. However, a mutualistic role benefiting both organisms cannot be excluded.

Unlike infections in arthropods, treatment of nematodes with antibiotics that are targeted at eliminating the *Wolbachia* infection also kills the host. This suggests that *Wolbachia* form an obligate mutualistic symbiosis with filarial nematodes, since neither organism can survive without the other. The exact nature of the mutualistic interaction is not known, but it has been proposed that *Wolbachia* provide the host with necessary nucleotides, cofactors and vitamins.

Despite maternal inheritance in arthropods, arthropod-borne *Wolbachia* do not evolve with the host. Instead, the bacteria are transmitted horizontally and infections are lost, although the mechanisms are not understood. In contrast, filarial nematodes and *Wolbachia* evolve together, reflecting the obligate symbioses between these bacteria and their hosts.

Interdomain lateral gene transfer

In 2001, Natsuko Kondo and colleagues described a variant of a bean beetle, *Callosobruchus chinensis*, where *Wolbachia* genes had moved into the insect chromosome. This movement of DNA from an organism

to an unrelated one is called lateral gene transfer (LGT). In filarial nematodes, an LGT event is responsible for the presence of two degenerate *Wolbachia* gene fragments in the nematodes *Onchocerca volvulus* and *O. ochengi*. It has also been proposed that mosquitoes acquired a *Wolbachia* gene involved in the resistance of *Anopheles* mosquitoes to *Wolbachia* infection. However, this claim is supported only by homology searches, which are inadequate to assign the directionality of LGT events. In fact, these proteins have only been found in *Wolbachia* and mosquitoes, making it impossible to assign directionality.

These are examples of interdomain LGT events, where DNA moves between two of the three domains of life (eukaryotes, eubacteria, archaea). Most described LGT events occur within a single domain of life. LGT is most common in eubacteria where it is responsible for movement of genes for antibiotic resistance, pathogenicity and bioremediation. A very striking example of interdomain LGT is in the hyperthermophilic eubacterial lineage *Thermotoga maritima*, which has 81 archaeal genes clustered in fifteen 4–20 kbp islands.

Interdomain transfers in higher multicellular eukaryotes are thought to be uncommon and unimportant, but several important cases have been documented. Most notably, the plant pathogen *Agrobacterium tumefaciens* transfers 10–30 kbp of T-DNA from the Ti plasmid (200–800 kb) to plants. Upon transfer, the T-DNA is targeted to the nucleus, incorporated into the plant chromosome by illegitimate recombination, and the genes are transcribed from eukaryotic promoters encoded in the T-DNA. Although normally associated with crown gall disease and subsequently the plant's death, this has also been used to introduce novel genes in plants (e.g. genetically modified crops).

Lateral gene transfers between *Wolbachia* and host chromosomes

In every genome sequencing project, sequences remain that do not end up in the final assembly and are often considered chaff or garbage. When combing through the chaff of the fruit fly *Drosophila ananassae* genome, we discovered numerous segments of DNA that belong to both *Drosophila* and *Wolbachia* genes. We verified the structure of some of these regions by PCR and demonstrated by *in situ* hybridization of polytene chromosomes that a large part of the *Wolbachia* genome has been integrated into the *D. ananassae* Hawaii 2L chromosome. Variably sized *Wolbachia* inserts were detected in four lines of *D. ananassae* from Asia and the Pacific, indicating that the insert may be widely distributed and degenerating. Lastly, we have found transcription of at least 28 *D. ananassae* genes of *Wolbachia* origin.

In the filarial nematode *Brugia malayi*, we characterized inserts in the whole-genome shotgun-sequencing project. As *Wolbachia* infection is required for the worm's fertility and development, the genomes of both organisms were sequenced simultaneously, complicating assemblies and leading to the removal of many *Wolbachia* reads during genome assembly (>98% identity over 90% of the read length on the basis of the independent BAC-based genome sequence of wBm, the *Wolbachia* endosymbiont of *B. malayi*). Despite this, the genome of *B. malayi* contains 249 contigs with *Wolbachia* sequences; PCR and end-sequencing confirmed nine of these inserts. The transfer of at least one region containing a degenerate fragment of the *Wolbachia* aspartate aminotransferase gene (Wbm0002), predates the divergence of three species, *B. malayi*, *B. timori* and *B. pahangi*. While the *D. ananassae* nuclear insert appears to be in one large piece, the *B. malayi* genome seems to have multiple inserts scattered through the genome with some large inserts of numerous *Wolbachia* genes, and other smaller inserts of a single gene fragment.

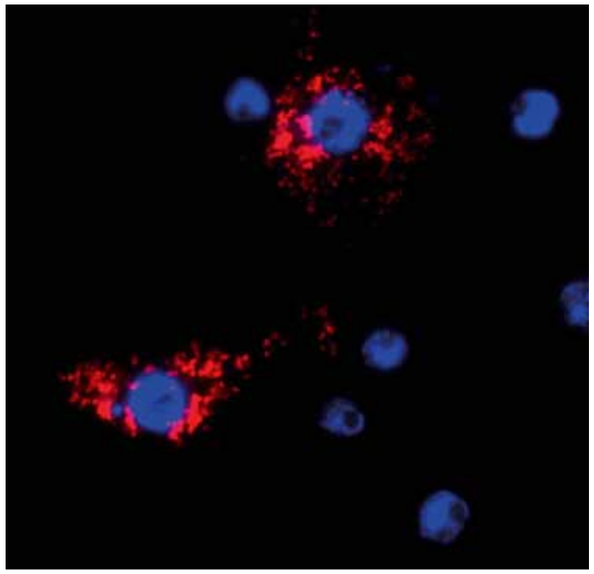
We have found numerous *Wolbachia* LGT inserts in the genomes of diverse invertebrate animals, including fruit flies, wasps and nematodes. Of 26 arthropod and nematode genomes in the trace repositories, 11 contain *Wolbachia* sequences. Of the *Wolbachia*-containing genomes, eight show evidence of having LGT between the endosymbiont genome and the host chromosomes. We have characterized host–endosymbiont LGT in five of these hosts. These results suggest that such inserts are common. Given that *Wolbachia* are among the most abundant endosymbionts, and their hosts represent the most abundant animal phyla, the view that interdomain transfers are uncommon and unimportant in multicellular organisms needs to be re-evaluated.

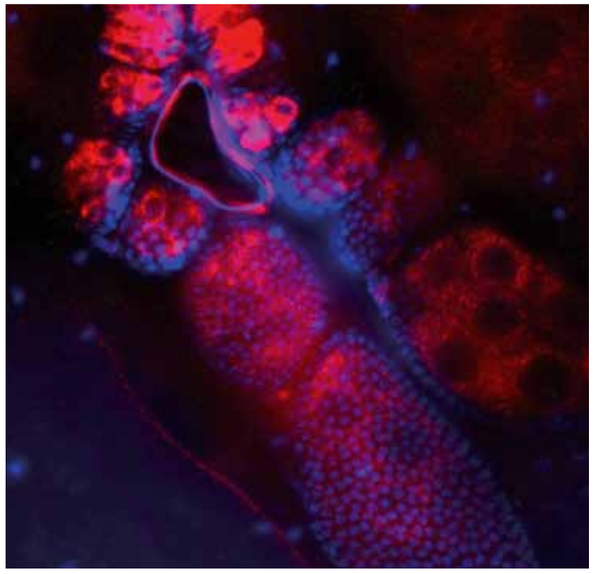
Endosymbiont lateral gene transfer ratchet

A lateral gene transfer ratchet has been proposed by W. Ford Doolittle to explain the accumulation of nuclear genes of organelle origin. The idea is that at some low frequency organelle genes will be inserted into the nuclear genome, and with some even lower frequency this will occur in positions that allow expression of the protein with an appropriate leader sequence for organelle targeting. Once this occurs, either the nuclear copy or the organelle copy will be lost. If the organelle copy is lost, the gene will become fixed in the nuclear genome, and as such becomes a successful transfer. Otherwise, the process can repeat itself, until all the genes that can insert in the nuclear genome have done so.

It seems reasonable to extend this theory to endosymbionts and their hosts. In the case of endosymbionts, a second option is available upon transfer of the gene to its host. If the genes transferred now fulfil the host's needs, the endosymbiont might become obsolete and can be lost. In the case of an obligate endosymbiont, this would result in the presence of endosymbiont-free lineages in clades of organisms with co-evolving obligate symbionts.

Such a situation exists in filarial nematodes that form an obligate mutualistic symbiosis with their *Wolbachia* strains. The origin of the symbiosis is thought to have arisen about 50 million years ago and occurred in the ancestor of the Onchocercinae and the Dirofilariinae, the *Wolbachia*-infected clades. However, since that time there appears to have been at least six independent losses of *Wolbachia* infection. Although *Wolbachia* infections can successfully be transferred to *Wolbachia*-free lineages, the infection is lost on culturing in animals, suggesting that the association is no longer stable. The nature of the instability has not been established. But it is plausible that an LGT event from the endosymbiont to the filarial nematode may have conferred the nematode with the ability to live without its once-obligate symbiont.





▲ Top. These cultured *Anopheles gambiae* Sua5B mosquito cells are infected with the *Wolbachia* strain wRi. The *Wolbachia* are red while the mosquito cell nuclei are stained blue. *Jason Rasgon*

▲ Bottom. These *Drosophila simulans* ovaries are infected with the *Wolbachia* strain wRi. The *Wolbachia* are red while the *Drosophila* cell nuclei are stained blue. *Jason Rasgon*

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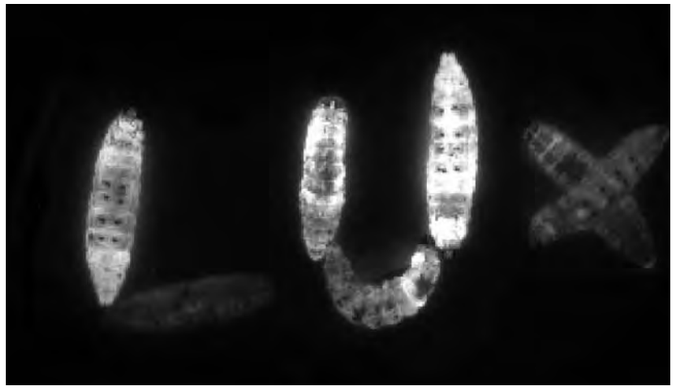
When living in a complex association with a nematode, the bioluminescent bacterium *Photorhabdus* can be deadly to insects, according to **Susan A. Joyce** and **David J. Clarke**.

Photorhabdus: shedding light on symbioses



▲ Insect larvae infected with *Photorhabdus luminescens* photographed in a dark room using the light produced by the bacteria. The insect hosts are final instar larvae of the greater waxmoth (*Galleria mellonella*). *Susan Joyce (Sand dunes, Photos.com/Jupiter)*

Next time that you are on the beach, walk into the dunes and take a sample of the sandy soil within the area where the dune grass is growing. Place your soil sample in a flask, add a few insect larvae (readily available from your local bait or pet shop) and the chances are good that the insects will be dead within 2–3 days. Take these dead insects into the darkest room in your house and within 5–10 minutes you should see that some, if not all, of the insect cadavers will glow in the dark. This bioluminescence is due to the presence of the bacterium *Photorhabdus*, a highly virulent insect pathogen (entomopathogen) that you have isolated in a nematode vector from the soil. Together, *Photorhabdus* and the nematode vector (*Heterorhabditis*) form a deadly complex that is naturally lethal to insect larvae.

Photorhabdus are members of the family *Enterobacteriaceae* and are, therefore, quite closely related to familiar pathogens such as *Escherichia coli*, *Salmonella*, *Yersinia* and *Erwinia* spp. To date three species of *Photorhabdus* have been described; *P. luminescens*, *P. temperata* and *P. asymbiotica*. Although *P. luminescens* and *P. temperata* only appear to infect insects *P. asymbiotica* has been found, in a relatively small number of cases, to be associated with infections in humans. These infections, although not fatal, do result in rather serious wounds that are difficult to treat. Fortunately, these cases appear to be restricted to the southern states of the USA (in particular Texas) and the Gold Coast of Australia. However, it is rather intriguing that, under certain conditions *Photorhabdus* does appear capable of 'jumping' from insect to human. Interestingly, in the laboratory, most strains of *P. luminescens* and *P. temperata* do not grow at temperatures >32°C, whilst *P. asymbiotica* can grow at 37°C. Therefore, perhaps the high ambient temperature of Texas and the Gold Coast has allowed *P. asymbiotica* to adapt to growth at the relatively high temperature of humans.

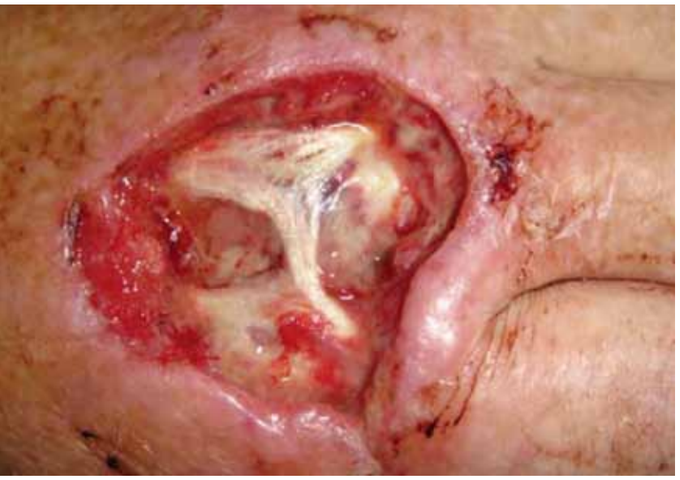
Comparing the genomes of insect and human isolates of *Photorhabdus* may uncover some interesting insights into the evolution of mammalian pathogenicity in environmental micro-organisms. To this end, the genome sequence of *P. luminescens* TT01 has been available since 2003 (http://genolist.pasteur.fr/PhotoList) and the genome sequence of a strain of *P. asymbiotica* has just been completed at the Sanger Centre (www.sanger.ac.uk/Projects/P_asymbiotica/).

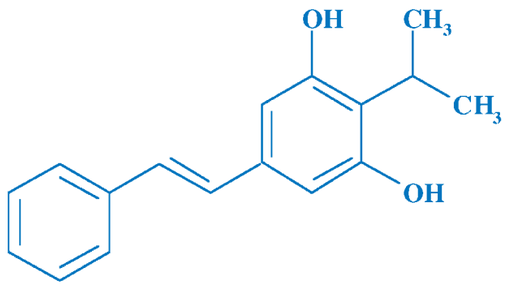
Bioluminescence

One of the most striking features of *Photorhabdus* bacteria is that they are bioluminescent and, indeed, it is this feature that gave the bacteria their name, i.e. *photo* (referring to the ability to produce light) and *rhabdus* (rod). *Photorhabdus* have a *lux* operon that contains all of the genes required for the production of light from fatty acids and molecular O_2, i.e. *luxCDABE*. The biochemistry of light production in bacteria is well described and it involves the conversion of a fatty acid into an aldehyde through the action of a fatty acid reductase (encoded by *luxC* and *luxD*). This reaction requires a supply of electrons that are delivered to the enzyme by the reduced electron carrier flavin mononucleotide (FMN). The aldehyde is then bound to the luciferase enzyme (encoded by *luxA* and *luxB*) which, together with O_2, forms an unstable ternary complex that rapidly decomposes, releasing H_2O, fatty acid and energy in the form of photons. The requirement for electrons suggests that one function of light production may be to act as an electron shunt that allows the recycling of essential electron carriers without the production of ATP and/or biomass. Although bacterial bioluminescence is quite common in the marine environment, *Photorhabdus* is the only terrestrial bacterium that is known to produce light. In the sea, many light-producing bacteria are involved in symbioses with marine animals and the role of bacterial bioluminescence can vary from protection (counter-illumination in the *Vibrio*–squid symbiosis) to the attraction of a mate. Unfortunately the role of bioluminescence in *Photorhabdus* is not yet understood, although, as all isolated *Photorhabdus* strains produce light, it is likely that there is a strong selection for this activity.

The life cycle

Photorhabdus are normally found colonizing the guts of the infective juvenile (IJ) stage of the nematode *Heterorhabditis*. The IJ is a soil-dwelling, motile, non-feeding stage of the nematode whose role is to actively seek out and infect susceptible insect larvae and release the *Photorhabdus* into the insect bloodstream. Here the bacteria begin to divide whilst producing a wide range of toxins and hydrolytic enzymes that serve to kill the insect within 2–3 days and facilitate the conversion of the internal organs and tissues of the insect into an environment where





▲ The molecular structure of 3′-5′-dihydroxy-4-isopropylstilbene (ST). *David Clarke*

◀ A hand infected with *P. asymbiotica*. *John Gerrard / Nick Waterfield*

the nematode can reproduce. During development, the nematodes feed on the *Photorhabdus* biomass within the insect cadaver and after 2–3 generations of reproduction, environmental conditions stimulate the development of IJs that are colonized by *Photorhabdus* before the IJ emerges from the insect cadaver into the soil. A single IJ infecting the insect will result in >100,000 IJs emerging from the insect cadaver 2–3 weeks later. The interaction between *Photorhabdus* and *Heterorhabditis* is, in effect, a highly effective symbiosis of pathogens and it is so effective that it is produced and marketed by several companies as a biocontrol agent for a variety of insect pests, in particular the weevil. Therefore, this bacterium has the ability to act as a pathogen in one host (insect) and a mutualist in another host (nematode).

Pathogenicity and toxin production

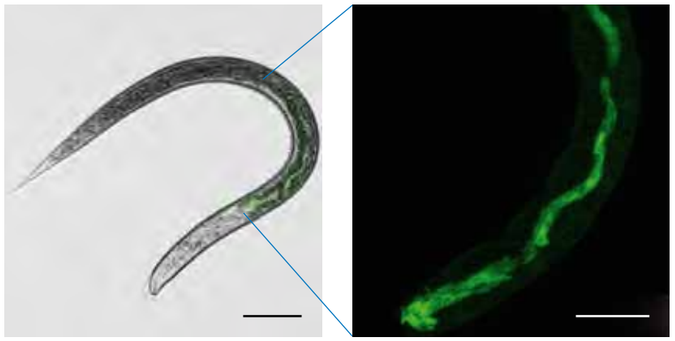
Photorhabdus is extremely virulent and, in some insect hosts, injection of a single cell is sufficient to kill the host within 2–3 days. *Photorhabdus* are capable of killing a wide range of insects from the Orders Coleoptera (beetles), Lepidoptera (moths, butterflies) and Diptera (flies). However, in the environment the host range appears to be limited by the ability of the IJ to penetrate the potential host. *Photorhabdus* grow exponentially in the insect, achieving high cell densities within the host [approx. 10^9 c.f.u. per *Galleria mellonella* (greater waxmoth) larva] and converting all of the internal organs and tissues of the insect into a biomass that is required for the growth and development of the nematode partner. There is a close correlation between the growth rate of *Photorhabdus* and the time taken to kill the insect, suggesting that pathogenicity is dependent on bacterial growth.

Insects have a very sophisticated innate immune system that has striking parallels with the innate immune system in vertebrates. This system is highly effective at killing bacteria, and *Photorhabdus* produce toxins that target the cellular branch of innate immunity. Analysis of genome sequence data has revealed that *Photorhabdus* encodes an impressive array of toxins. Indeed studies in *Photorhabdus* have resulted in the identification of a new family of toxins that have since been shown to be found in other bacteria, including mammalian pathogens. The Tc toxins from this family are large protein complexes that can be poisonous when fed to insect larvae. When cloned into the model plant *Arabidopsis*, the Tc toxins provide protection against insect pests, suggesting a potential alternative to Bt toxin.

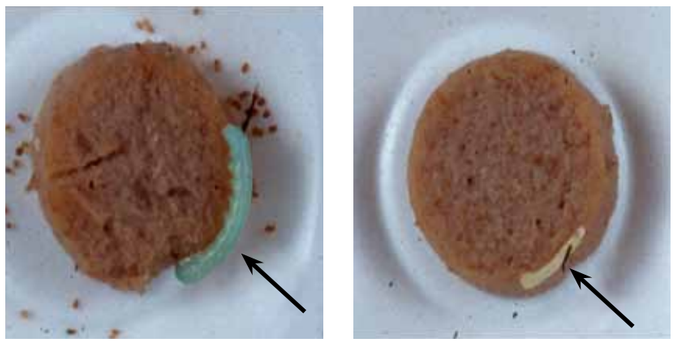
Mutualism and signal production

The *Photorhabdus–Heterorhabditis* association is highly specific, and nutritional interactions do make a contribution to this specificity. Therefore, a particular isolate of *Heterorhabditis* cannot feed on all *Photorhabdus* bacteria. Nutritional interactions are common in many mutualistic associations, e.g. amino acid exchange between plant cells and *Rhizobium bacteroides*, but the details of these interactions are not yet known in the *Photorhabdus–Heterorhabditis* system. In addition, successful colonization of the IJ is essential for both partners in the association, and it has been shown that IJs will only be colonized by the nematodes' cognate bacterial partner (or in some cases a very close relative). *Photorhabdus* is transmitted to the IJ via the mother in a very complex process that results in her infection and death.

During the stationary phase of growth, *Photorhabdus* produces several small bioactive molecules, including a redox-active, anthraquinone pigment and a stilbene molecule, 3′-5′-dihydroxy-4-isopropylstilbene (ST). The ST molecule is produced in large quantities when *Photorhabdus* are grown in either LB broth or insect larvae, and it was originally identified as an antibiotic. It was suggested that



◀ GFP-tagged *Photorhabdus* in the gut of a *Heterorhabditis* IJ. Bars, 50 µm (left) and 20 µm (right). *Catherine Easom*



▼ The Tc toxins are orally toxic to larvae of *Manduca sexta* (the tobacco hornworm moth). In a typical bioassay, 2nd instar insect larvae are allowed to feed on a wheatgerm-based diet that can be treated with preparations of the Tc toxin complex. The larvae do not feed on the food with the Tc complex added (right) and fail to develop compared with controls (left). *Nick Waterfield*

the role of ST was to protect the insect cadaver from saprophytic organisms in the soil. However, recent studies have shown that ST is also an inter-kingdom signal that is involved in controlling the development of *Heterorhabditis* into the IJ stage. The IJ is developmentally analogous to the dauer stage in the model nematode *Caenorhabditis elegans*. In *C. elegans*, dauer formation is a response to the low availability of food and/or high nematode numbers. Therefore, it is possible that ST is perceived by *Heterorhabditis* as an indication that food (i.e. bacteria) is plentiful. The ST molecule is multipotent and has also been shown to dampen the insect immune system so that the nematode and bacteria are invisible to the insect immune system post-infection.

The future is bright (or should that be light-producing!)

Photorhabdus is a Gram-negative bacterium that is equipped for life as a mutualist in one host and as a pathogen in another, including the occasional human. Its complex life cycle, relatedness to important mammalian pathogens and amenability to genetic manipulation have contributed to the development of this genus as an exciting model for studying bacteria–host interactions. However, *Photorhabdus* is also quickly emerging as a source of novel bioactive compounds. In total there are 22 genetic loci in the genome of *P. luminescens* TT01 that contain genes predicted to be involved in the production of small bioactives, including polyketide synthases (PKS), non-ribosmal peptide synthases (NRPS) or PKS-NRPS. These loci occupy 7% of the TT01 genome compared to 4% in *Streptomyces*, the organism responsible for the production of many important antibiotics. Therefore, it is expected that screening libraries of *Photorhabdus* DNA will identify new bioactive compounds, including toxins and antibiotics.

From a more fundamental perspective, we expect that the tripartite interaction between *Photorhabdus*, *Heterohabditis* and insect will also help us to answer a very important question: what is the real role of such bioactive molecules in nature?

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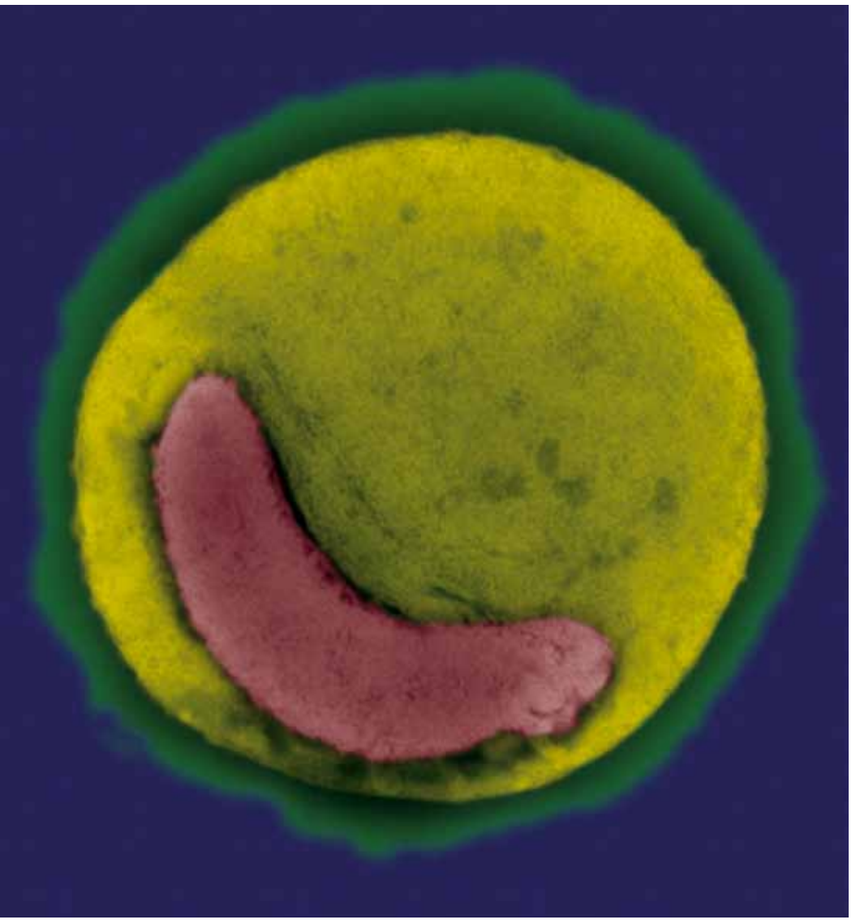
An inside job: *Bdellovibrio bacteriovorus*

Some predatory 'bugs' eat other 'bugs' from inside, as **Liz Sockett** and her research group have found.

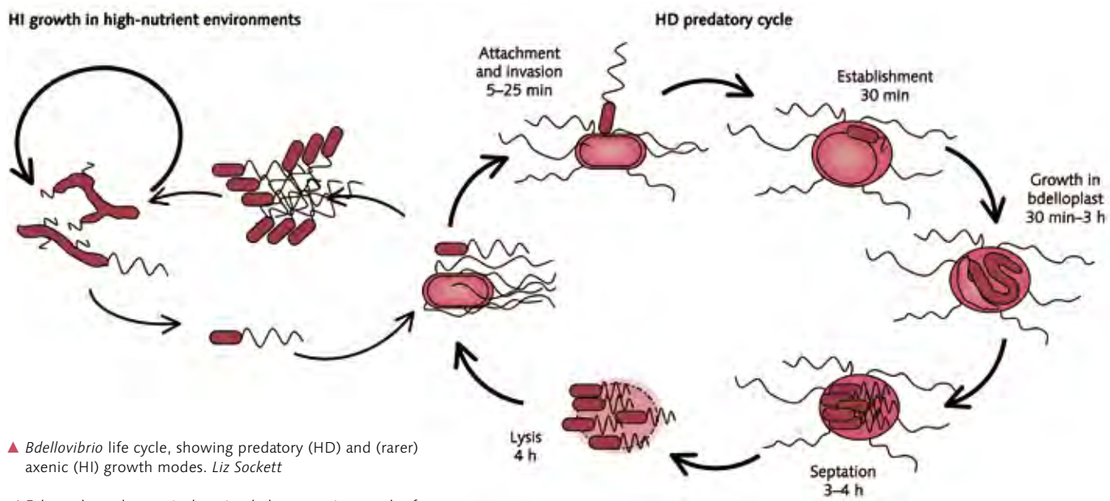


Bdellovibrio are small (0.25× 1.0 µm), flagellate, motile, Gram-negative deltaproteobacteria which invade and kill other Gram-negative bacteria, entering the prey cell's periplasm, replicating within it and using the contents of that bacterium as their nutrient source. *Bdellovibrio bacteriovorus* HD100 is the sequenced strain and has a 3.8 Mb genome, indicating that although *Bdellovibrio* have evolved to invade and 'eat' other bacteria, they have not lost large numbers of genes, as is the case with truly parasitic bacteria which rely on their hosts. The interaction between *Bdellovibrio* and other bacteria can be thought of as predatory rather than parasitic as, in most cases, the *Bdellovibrio* kill the prey cell within 15 minutes of entry and do not establish a long-lived parasitic relationship within it.

In keeping with its large genome, *B. bacteriovorus* can exist in two different growth phases, as host-dependent (HD) cells that require prey for growth and division, and as host-independent (HI) cells, when growing in rich nutrient media as might be found in biofilms and sediments in nature. The balance between HD and HI growth in natural environments is not known, but HI growth is a useful tool for saving non-predatory mutants for study in the lab setting. Predatory growth seems to be a kind of evolutionary trade-off in *Bdellovibrio* where the acquisition of a large number of genes for hydrolytic enzymes, and for penetrating and resealing the prey cell, give access to an intracellular niche, bounded by the prey-cell outer membrane, where the *Bdellovibrio* can 'dine privately' on the inner contents of the prey cell without competition for nutrients from other bacteria. This contrasts with the 'eating habits' of other deltaproteobacteria such as the myxobacteria which digest prey externally and take up digested prey nutrients partly in competition with other bacteria in their surroundings.

Predatory growth

When growing predatorily, *Bdellovibrio* exhibit a biphasic lifestyle with a free-swimming attack phase and a sessile intraperiplasmic growth phase, during which they reside inside the dead prey cell, degrading it by secreting enzymes across the prey cytoplasmic membrane to digest prey macromolecules, and taking up the products for *Bdellovibrio* growth. *Bdellovibrio* seem to be mostly 'locked on' to predatory growth in dilute environments and cannot productively switch to HI growth to survive, but depend on finding prey for replication. During the free-swimming attack phase, rapid prey location, attachment and recognition are vital to the successful replication of the *Bdellovibrio*, as they typically have a half-life of about 10 hours during starvation in buffered environments. A large complement of genes for flagellar and chemotaxis systems is seen in the genome to aid movement towards prey-rich regions.



▲ *Bdellovibrio* life cycle, showing predatory (HD) and (rarer) axenic (HI) growth modes. *Liz Sockett*

◀ False-coloured, negatively stained electron micrograph of a *B. bacteriovorus* bdelloplast. *David Milner and Laura Hobley*

Bdellovibrio attach to many kinds of surfaces reversibly, including inorganic particles and Gram-positive cells (which are not prey as they do not have a periplasm). How they tell prey from 'junk' is unknown. There seems to be a brief recognition period, during which the *Bdellovibrio* cell identifies its prey, attachment between *Bdellovibrio* and prey becomes irreversible, and the *Bdellovibrio* begins its invasion process. A small pore is produced in the outer membrane of the prey, through which the *Bdellovibrio* bacterium seems to squeeze. Once inside, the pore is resealed, and modification of the prey's peptidoglycan causes the rounding of the prey cell and the formation of a structure called a bdelloplast. This is followed by the intraperiplasmic hydrolysis of prey, as mentioned above. The *Bdellovibrio* cell elongates, and then septates at multiple fission sites. The multiple progeny cells become flagellate, before releasing a final wave of lytic enzymes to burst from the confines of the bdelloplast and seek out more prey.

We and others are actively engaged in functional analyses of the genes within the *B. bacteriovorus* HD100 genome, studying expression patterns and defining roles for them in the *Bdellovibrio* life cycle. We have shown that, although *Bdellovibrio* swim actively using chemotaxis to find prey-rich regions, they do not use actively rotating flagella to 'bore' into prey. We have found that preventing expression of the *Bdellovibrio* PilA fibre protein of Type IV pili abolishes prey entry, showing that pili are involved in productive prey attachment and or penetration.

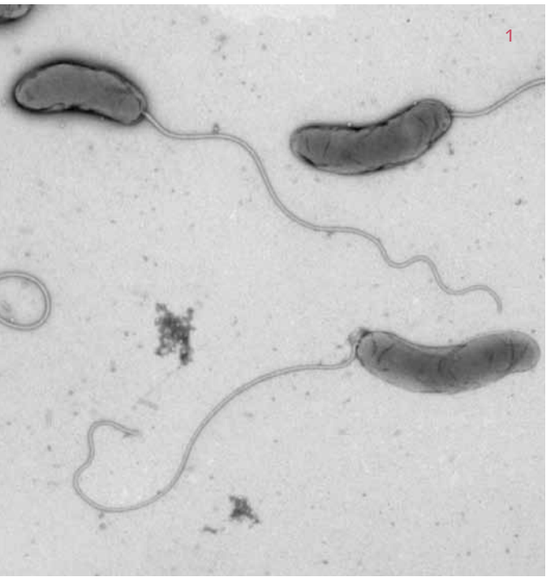
Where are *Bdellovibrio* found?

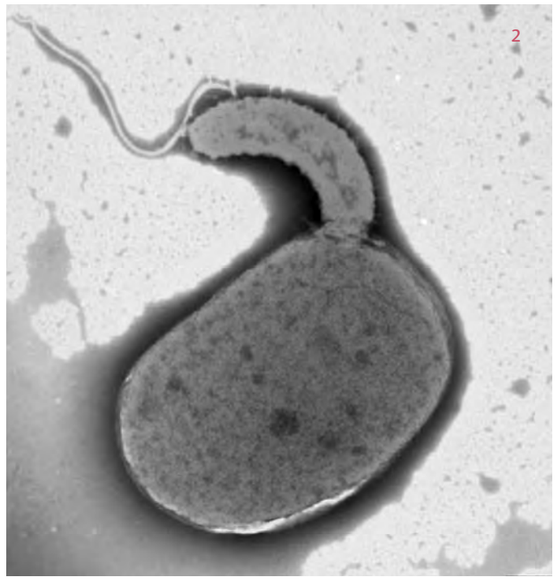
Bdellovibrio are found throughout nature; wherever there are suitable prey to be 'eaten', *Bdellovibrio* are usually found eating them! Soil and fresh water samples are often found to contain *Bdellovibrio*, or its closely related cousins *Bacteriolyticus* and *Peredibacter*, whilst salt-water samples often yield *Bacteriovorax* spp., another closely related cousin. *Bdellovibrio* have also been isolated from sewage, and from the gut flora of humans, horses and chickens. *Bdellovibrio* 16S rDNA sequences have been found in a variety of metagenomic studies, including those from marine sediments and even human skin. *Bdellovibrio* are found strongly associated with natural biofilms, and recent studies have shown that effective predation occurs in these naturally occurring bacterial communities.

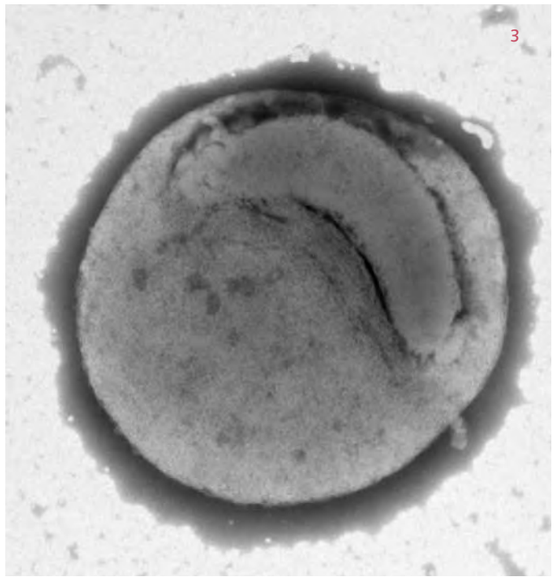
Living antibiotics!

In July 2008, the Health Protection Agency published further worrying statistics about the rise of antibiotic-resistant Gram-negative infections in the UK, charting the levels of resistance particularly in pathogenic *Escherichia coli* species. *Bdellovibrio* naturally attack and kill a wide range of pathogenic Gram-negative bacteria, including *Salmonella*, *E. coli*, *Proteus*, *Pseudomonas*, *Burkholderia*, *Serratia* and others. If applied as 'living antibiotics', *Bdellovibrio* would avoid many of the shortcomings of phage therapy which utilizes bacteriophage as a treatment against bacterial infection. *Bdellovibrio* are not known to be prey-specific; they infect a variety of Gram-negative hosts, and have no known specific host recognition sites. In contrast, bacteriophage attach to specific molecular targets, hence are only effective against a narrow range of bacteria, which can in turn become resistant by simple point mutations in genes encoding these protein targets. In addition, some phage are unable to invade cells with capsules, whereas bacterial capsules have been shown to be an ineffective barrier to predation by *Bdellovibrio*. *Bdellovibrio* have been shown to be unable to enter and infect mammalian cells, which is of great importance when considering their potential as an antibiotic treatment. This means that they could infect and kill the pathogenic bacteria causing the infection whilst not causing harm to a patient.

The potential applications of *Bdellovibrio* offer an exciting avenue for further research, and may one day form part of a new generation of antimicrobial therapeutics. In the future you may visit a doctor and be prescribed '*Bdellovibrio* therapy' to combat your infection!







▲ Negatively stained electron micrographs of *Bdellovibrio bacteriovorus* HD100.
(1) Free, motile, attack-phase swimming cells hoping to encounter Gram-negative bacterial prey. The cells have long sheathed flagella with an unusual wave-form caused by the presence of several different flagellin proteins making up the flagellum.
(2) Attaching to Gram-negative bacterial prey for invasion through the prey outer membrane.
(3) Living within bacterial prey forming a bdelloplast where the prey bacterium is beginning to be consumed and the *Bdellovibrio* is starting to elongate and grow prior to replication.
Andrew Fenton, David Milner and Laura Hobley

Liz Sockett, Laura Hobley, Andrew Fenton, Richard Woods, Carey Lambert, Chien-Yi Chang, Robert Atterbury, Rob Till, Marilyn Whitworth, Mike Capeness, Rowena Fung, Rashidah Ahmad, David Milner, Tom Lerner & Simon King
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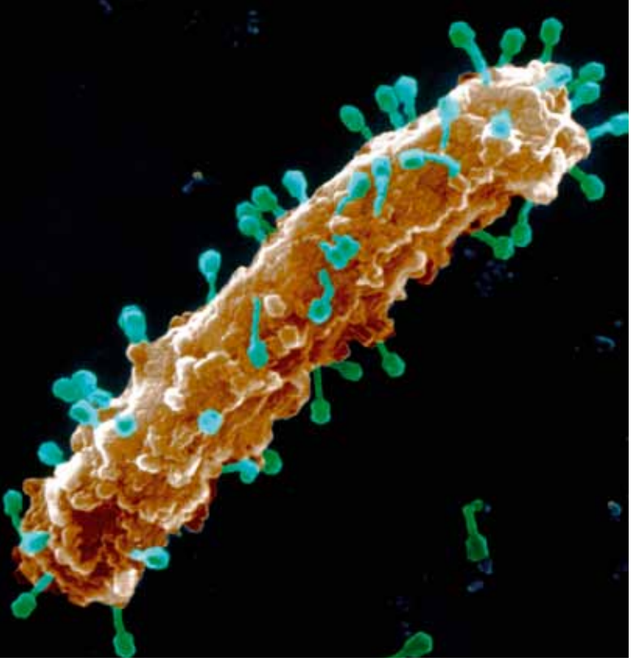
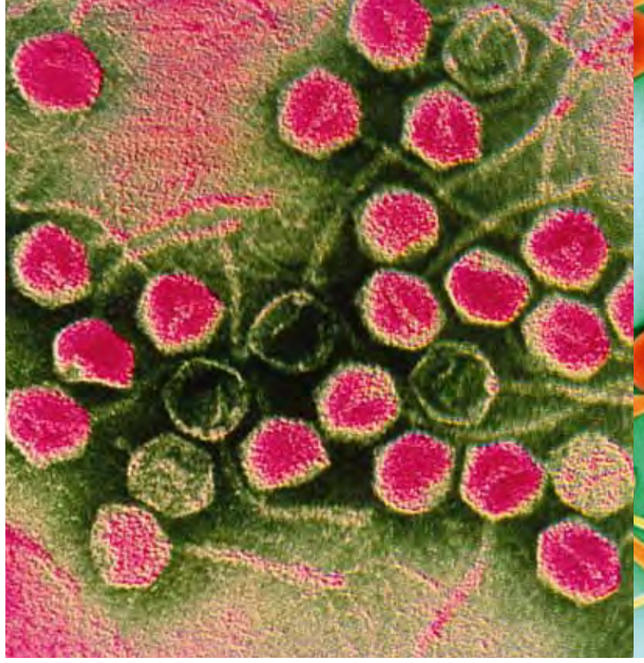
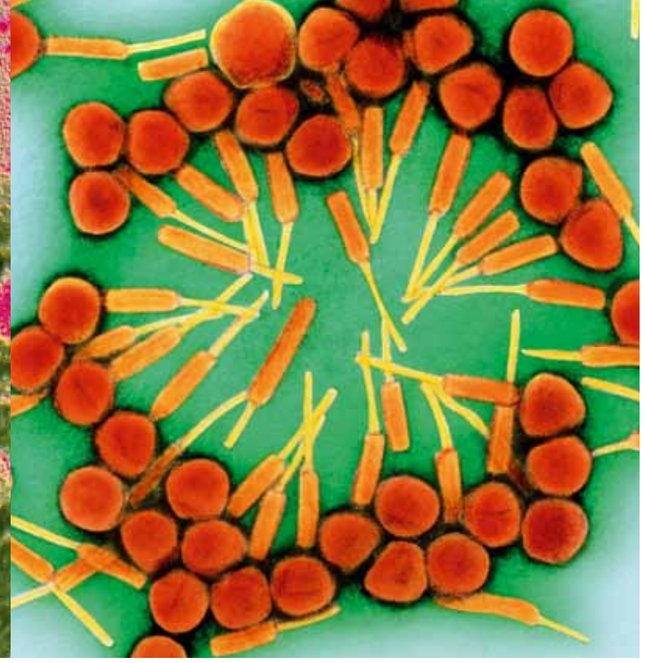
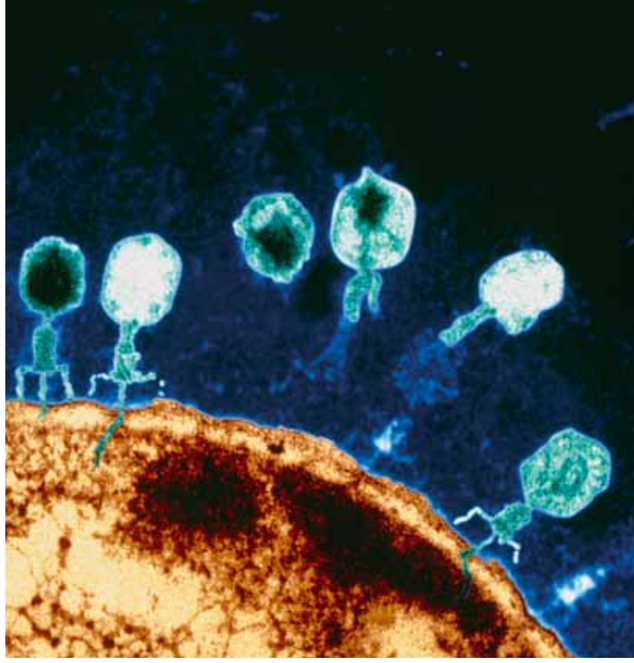





Bacteriophages: nature's most successful experiment

Phages exist on our planet not only in huge numbers but infinite variety as **Graham F. Hatfull** describes.

▲ Coloured electron micrographs of a variety of bacteriophages. *From left to right*: SEM of T phages attacking *Escherichia coli* (*Eye of Science / SPL*); TEM of lambda phages (*CNRI / SPL*); TEM of a cluster of P1 phages (*Biozentrum / SPL*); TEM of T phage particles attacking *E. coli* (*Eye of Science / SPL*).

You may well be under the impression that the largest number of undiscovered species – and the greatest pool of unknown genes – lie within the considerable biodiversity of the tropical rain forests. Not so. A compelling argument can be made that the biggest reservoir of unidentified genetic information is all around us, in the global population of bacteriophages.

How many phages are there?

There are two main components to this conclusion: the amazing abundance of phages in the environment and the emerging picture of their genetic diversity. Over the past few years it has been calculated that the total number of phage particles in the biosphere is a stunning 10^{31}. This is a remarkable number, because it suggests that phages are a numerical majority of all biological entities – i.e. there are more phage particles than all other biological forms added together. If abundance can be equated with success, then phages represent the result of nature's most successful experiment! It is helpful to understand how this abundance is calculated. Samples from the environment can be stained with dyes that cause viruses and bacteria to fluoresce, and the number of particles counted using fluorescent microscopy. There are two main observations: that viral particles are typically present at 10^6–10^7 per ml seawater, and that there are 5- to 10-fold more viruses than bacteria. The viral abundance is broadly similar whether seawater or terrestrial samples are analysed, and does not change significantly when comparing coastal, oceanic, surface or deep-water samples. A simple extrapolation to the total volume of seawater and inclusion of terrestrial counts leads to a total number of phage particles of 10^{31}. An independent estimate of the total number of bacteria in the biosphere arrived at 10^{30}, providing some comfort in the validity of these estimations.

A dynamic population

The abundance of phage particles is impressive, but would be rather less interesting if these were just a large number of a small number of types. However, there are clues suggesting that this is not the case. First, it has been estimated that there are approximately 10^{24} viral infections of bacteria per second on a global scale, suggesting that the entire phage population turns over every few days – far from being static, the population is highly dynamic, with each cycle of infections having the potential to generate altered or mutant particles. Second, it seems likely that the evolutionary origin of phages is not too distant from that of their bacterial hosts, so this dynamic relationship has been going on for at least 2 billion years!

What type of viral population has arisen, what do they look like, and how different are their genomes? Phages were among the first 'invisible' entities to be observed by electron microscopy, which showed them to be well-defined structures containing a protein head (capsid) surrounding the genetic material, attached to a tail. While these tailed phages containing double-stranded DNA (dsDNA) are perhaps the most common forms, a large variety of different morphotypes have been described, with some spectacular shapes described recently for viruses of archaeal hosts. The genetic material in phages can be either DNA or RNA, either in single- or double-stranded forms.

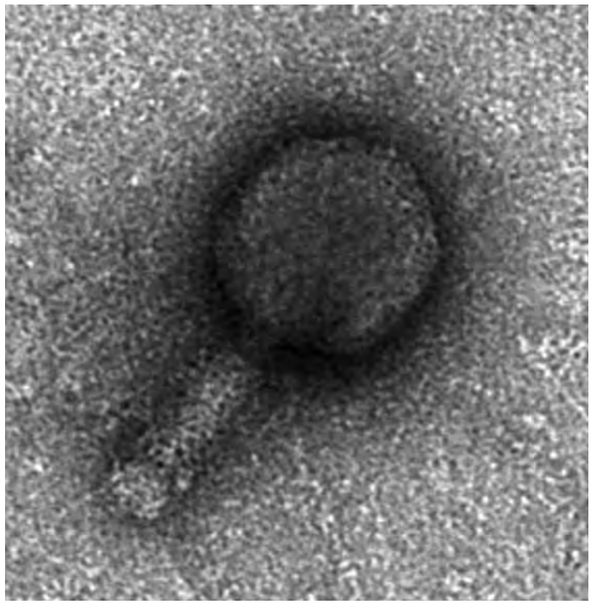
Genomics

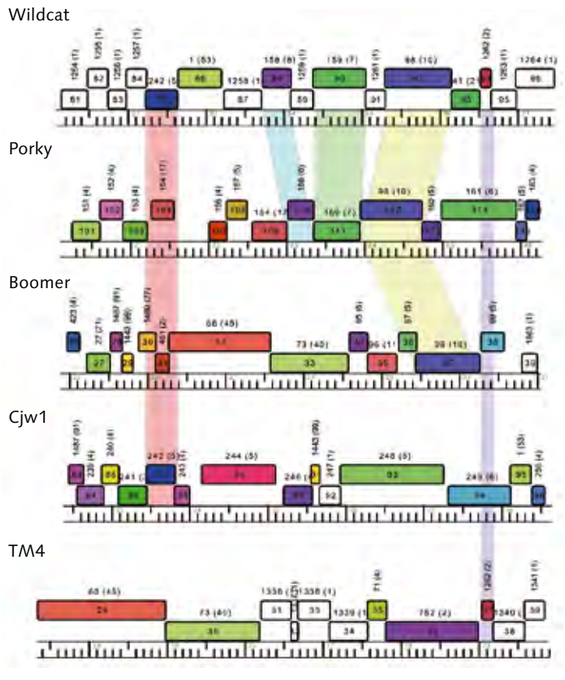
Currently, just over 500 completely sequenced phage genomes are listed in the Genomes section at the National Center for Biotechnology Information (NCBI). The size of this collection has grown considerably over the past 5 years, but is still dwarfed by the number of sequenced bacterial genomes (currently ~750), even though these are 100 times larger. While these sequenced phage genomes represent only a

tiny slice of the total phage population, their comparative genomic analysis has provided some fascinating insights into the diversity of the population and the evolutionary mechanisms generating this diversity.

There are two general ways of thinking about the genetic relationships within the phage population. One is to consider the similarities between groups of phages that infect different bacterial hosts; the other is to compare genomes of phages that infect a common bacterial host. The 500 sequenced phage genomes correspond to about 70 different bacterial hosts (a small subset of the ~470 bacterial species that have been sequenced), and because phages probably exist for the vast majority of bacterial species, this is likely to correspond to a small and highly unrepresentative sample. Nonetheless, comparisons of these genomes show that they are highly diverse, and phages of one bacterial host will often have little or no recognizable nucleic acid sequence similarity with phages of other hosts. Although amino acid sequence comparison of predicted gene products can detect more distant relationships, relatively few genes emerge as having common evolutionary origins. However, it appears as though the more closely related the bacterial hosts, the greater the chance that their phages may share common genes. For example, phage PA6 of *Propionibacterium acnes* contains a number of genes that are shared by phages of the mycobacteria. Overall, it seems reasonable to suppose that phages form a continuum of relationships that will only be fully understood with a substantial increase in the number of sequenced genomes.

Substantial groups of sequenced genomes have now been accumulated that share common hosts, with more than 20 genomes for each of *Burkholderia*, enterobacteria, lactococci, mycobacteria, pseudomonads, staphylococci and streptococci. An emerging theme is that these groups are also quite divergent, although there are clusters of phages that are more closely related to each other than to others of that host. This probably reflects a similar, but perhaps more focussed view to that of the phage population as a whole, with the clusters probably representing unequal sampling





▲ Virion morphology of mycobacteriophage Bxz1. Electron microscopy shows that Bxz1 contains an icosahedral capsid containing a dsDNA genome, and a contractile tail. *Graham Hatfull*

▶ Mosaicism in mycobacteriophage genomes. Short segments of five mycobacteriophage genomes are shown with the genes represented as coloured boxes. Each gene has been assigned to a phamily (Pham) of related sequences and the Pham number presented above the box, along with the number of genes in that Pham in parentheses; genes of the same Pham are coloured accordingly. Genes without any relatives elsewhere in the collection of 50 completely sequenced mycobacteriophage genomes are shown as white boxes. Phages Porky, Boomer, Cjw1 and TM4 all contain at least one gene that is related to one in Wildcat in this region, and coloured stripes indicate these relationships. Careful inspection will reveal additional genes shared by some of these phages. *Graham Hatfull*

of the population rather than specific and stable population structures. Viral metagenomic studies – in which DNA fragments from the total collection of viruses in a sample are sequenced – support this view of a highly diverse phage population.

Mosaicism

One of the clearest and most amazing aspects of phage genomes is their mosaic architecture. Comparative analysis reveals segments or modules that are shared by two or more phages, but which are flanked by different modules These modules can be groups of genes – especially those whose functions need to work together, such as the virion structural genes – or single genes. In the mycobacteriophages, this single-gene mosaicism within the non-structural genes is particularly prevalent with large groups of contiguous genes having distinct and different evolutionary histories. The diversity of phage genomes suggests that the number of different modules is very large and that only a very small subset have as yet been identified. Each individual phage genome can thus be viewed as a unique assembly of modules, and the combinatorial possibilities are enormous.

Evolutionary mechanisms

The evolutionary mechanisms that give rise to these mosaic genome structures is not clear, although both homologous and illegitimate recombination appear to be involved. One particular mystery is how the junctions between modules are generated, and although these could arise from homologous recombination between short conserved boundary sequences, these are not found in most phage genomes. An alternative explanation is that illegitimate recombination occurs at randomly chosen positions and with randomly chosen partners, which could be other phage genomes, plasmids or the bacterial chromosome. Most of these events will generate genomic trash, but with selection for appropriately-sized genomes that can be packaged into capsids, and for maintenance of a functional set of genes, viable progeny could arise. The overall process is not expected to be efficient or frequent, but with such a dynamic population evolving over such a long period of time, this would not seem to be a problem. Other events such as transposition and site-specific recombination events will also generate further rearrangements, and homologous recombinationl mediates exchanges at common gene sequences.

Gene functions

What do all these phage genes do? While the genes required for virion structure and assembly can often be recognized – especially since they are often arranged in common gene orders – along with some recombination and DNA replication activities, the functions of most other phage genes remains largely unknown. When they are compared against databases such as GenBank, matches revealing putative functions are relatively rare, and typically fewer than 30% of genes in newly sequenced phage genomes can be assigned putative functions. Genomics and bioinformatics are thus unlikely to provide a comprehensive understanding of phage gene functions, and experimental approaches are clearly needed.

Phage genomics are clearly in their infancy. The current state of the field provides a tantalizingly tasty appetizer, but with such a vast landscape of unexplored phages yet to be studied, one cannot but feel that the main course is yet to come. In the next few years, the advent of ultra-high throughput DNA sequencing technologies will generate a multitude of new phage genome sequences, and functional and structural genomic approaches will help us to elucidate their biology. While we may never know for sure what the whole phage population looks like, perhaps we can at least learn enough to appreciate how much of it we really don't understand.

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1983: a vintage year for pathogen discovery

The SGM President, **Robin Weiss**, recalls the year in which three important pathogens first saw light of day.

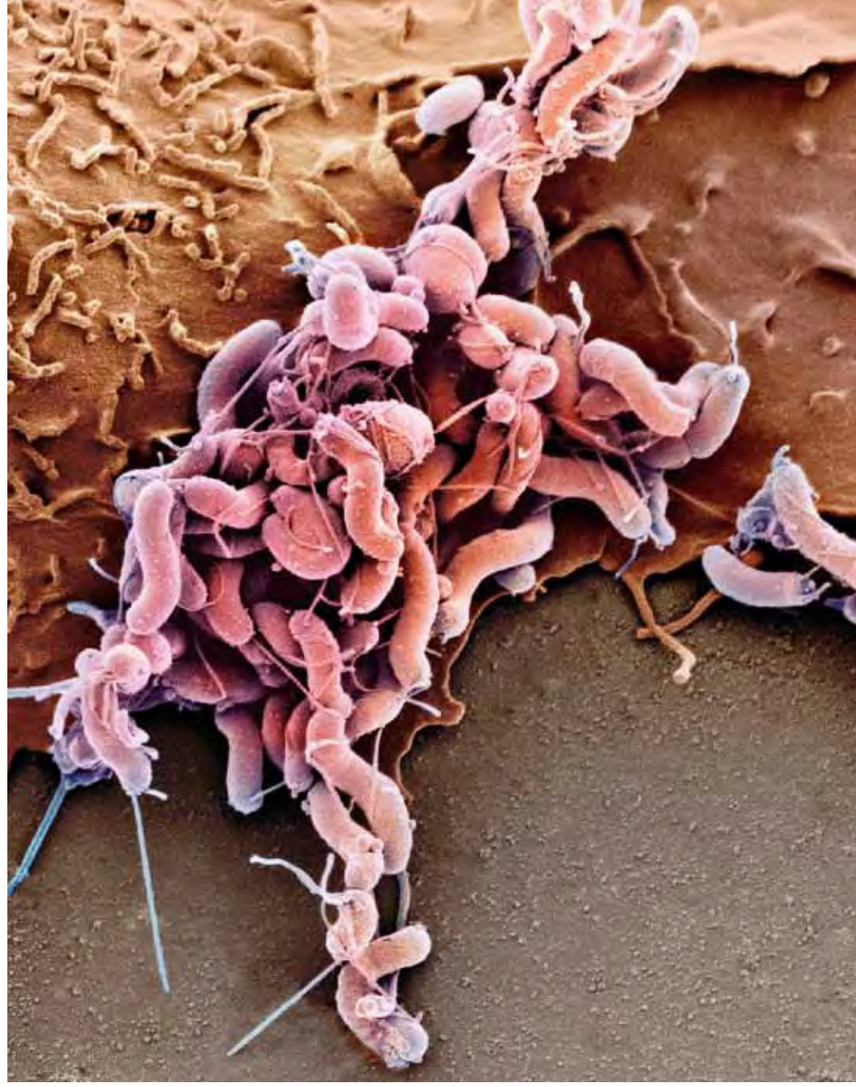
This year marks the 25th anniversary of three independent discoveries concerning human infectious diseases. In 1983, *Helicobacter pylori* was found to be associated with stomach ulcers by Robin Warren and Barry Marshall, human papilloma virus (HPV) type 16 was identified as a candidate agent of cervical cancer by Harald zur Hausen's group, and human immunodeficiency virus (HIV) was first isolated from a patient with symptoms suggestive of the early stages of AIDS by Françoise Barré-Sinoussi, Luc Montagnier and colleagues. Although these pioneering discoveries were initially greeted with scepticism, each has stood the test of time.

Gastric ulcer and dyspepsia were never considered to be caused by an infectious agent before the discovery of *H. pylori* (initially called *Campylobacter pylori*). While bacteria had been occasionally observed in the stomach since the early 20th century, this part of the gastrointestinal tract, together with the small intestine, was generally considered to be sterile. Neither did the epidemiology of gastric ulcer disease point towards an infectious agent, although wide variance in geographic prevalence was noted. *H. pylori* was later also shown to be the underlying cause of duodenal ulcers, stomach cancer and mucosa-associated lymphoid tumours.

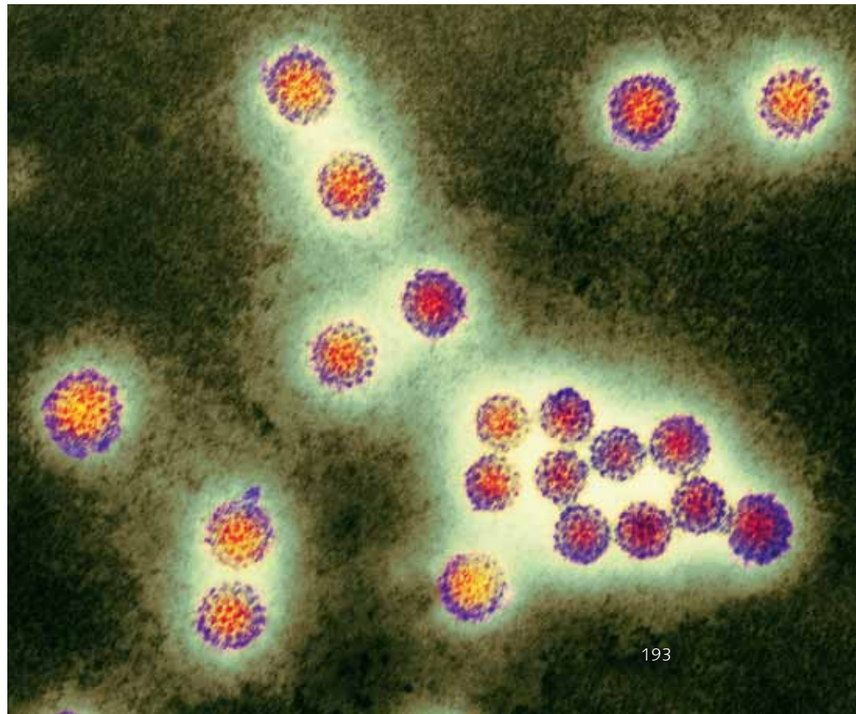
Warren and Marshall faced an uphill battle to persuade GI specialists that the majority of peptic ulcers had a bacterial aetiology. Barry Marshall resorted to a time-honoured and dramatic method of testing one of Koch's postulates on himself. He swallowed a culture of the bacteria and promptly developed severe dyspepsia. He also showed that treatment of ulcer patients with inexpensive antibiotics often cured the illness altogether. For too long the treatment of ulcers by antibiotics was strongly opposed by pharmaceutical companies which sold far more expensive drugs for the chronic treatment of the symptoms, e.g. H2-receptor antagonists.

In contrast to gastric ulcer, cervical carcinoma had long been thought to result from a sexually transmissible agent. In 1842, an astute gentleman of Verona, Domenico Rigoni-Stern, observed that while nuns had an increased incidence of breast cancer, they seldom developed cervical cancer, whereas the latter was a frequent disease among prostitutes. When the hunt was on for human cancer viruses following the discovery of Epstein–Barr virus in Burkitt's lymphoma in 1964, several investigators implicated herpes simplex virus type II as the cause, but the epidemiology was inconclusive. Genital HPV strains were the first viruses to be discovered through DNA cloning because they were not amenable to classical isolation through cell culture. Zur Hausen cloned HPV-6 and HPV-11 in vulval papillomas and used an HPV-11 probe to pull out HPV-16 and then HPV-18 from malignant cervical carcinoma. Cloning methods were subsequently used to identify many other non-culturable human viruses, such as hepatitis C virus, Kaposi's sarcoma herpesvirus and this year, a novel polyoma virus in Merkel cell carcinoma.

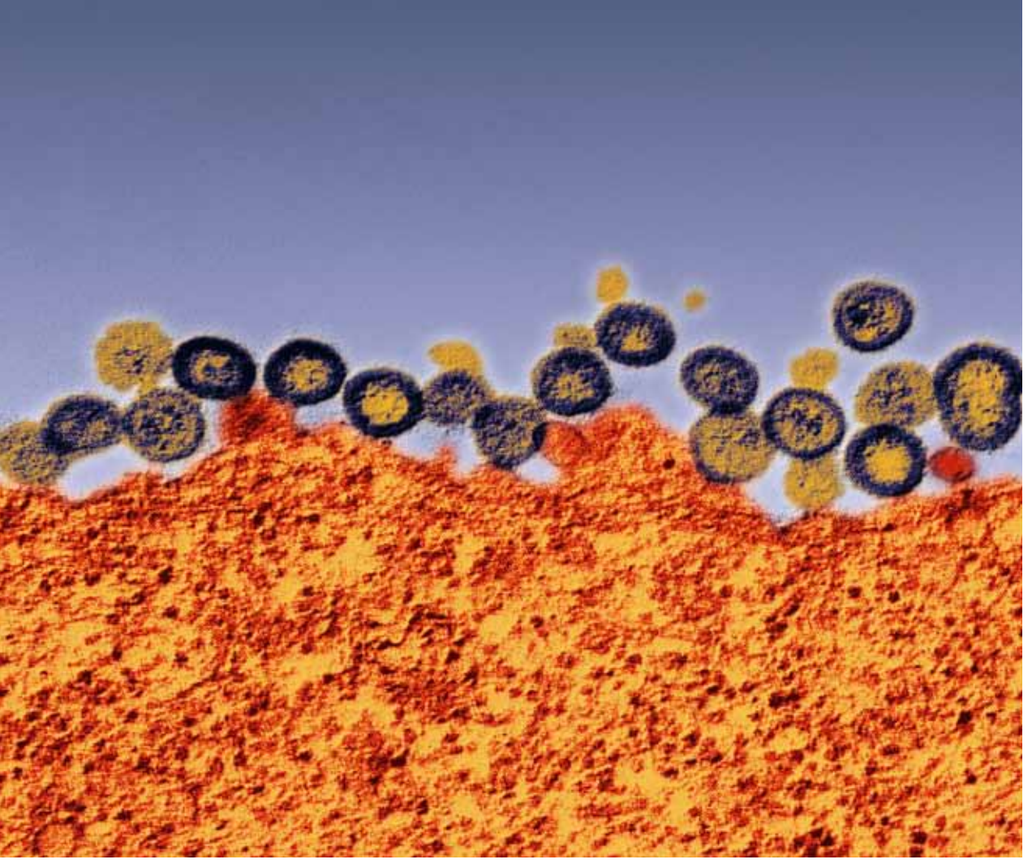
The discovery of genital HPVs led to the recent development of two vaccines that prevent infection by the most prevalent cervical HPV strains.



▶ Coloured SEM of *Helicobacter pylori* bacteria (pink) on human gastric epithelial cells (light brown). *Science Photo Library*



▼ Coloured TEM of HPV virions. *Centre for Infections / HPA / Science Photo Library*



◀ Coloured TEM of HIV particles (blue and yellow) budding from the membrane of a cell. *Dr Klaus Boller / Science Photo Library*

The vaccines are based on virus-like particles containing no genomes which self-assemble from recombinant coat protein and act as efficient immunogens. Hopefully, cervical cancer will eventually become a rare curiosity rather than the most common women's cancer.

Whereas HPV and *H. pylori* represent ancient human infections that have newly emerged to human knowledge, HIV-1 is a genuine newcomer, having transferred from chimpanzees within the last 100 years. AIDS was first recognized in 1981 in gay men in the USA who developed *Pneumocystis carinii* infection or Kaposi's sarcoma. The appearance in Africa around the same time of what was called 'slim' disease heralded the seriousness of the HIV pandemic. When HIV-1 was discovered in May 1983, epidemiologists already knew that the underlying cause of AIDS was an agent transmissible by sex, blood and blood products, and from mother to child. Different investigators had championed various candidate agents, such as leukaemogenic retroviruses, herpesviruses and papilloma viruses, or a fungus in the gut that might release an immunosuppressive product like cyclosporine. So it was not immediately clear whether Barré-Sinoussi and colleagues had found the genuine culprit – through classical propagation in cell culture. However, the French team then made further isolates from AIDS patients, showed that the virus was cytopathic in CD4+ T cells but not other cells, and noted that it resembled a lentivirus. One year later, Bob Gallo in the USA made his own claims to the discovery of HIV, but he had, in fact, confirmed those of the Insitut Pasteur. Gallo had discovered the first human retroviral pathogen, human T-cell leukaemia virus in 1980, which in itself was a major milestone.

The discovery of HIV had an immediate impact on public health through the development of diagnostic tests which were rapidly introduced for screening tainted blood donations. Treatment with anti-retroviral drugs has proved to prolong the length and quality of life, but as with antibiotics, drug-resistant strains of HIV emerge. Alas, an efficacious vaccine to protect against HIV infection is not yet in sight, though not for want of trying.

Each of these discoveries 25 years ago was a leap forward in our understanding of persistent infections that lead to disease in humans, often years after the initial infection event. In 2005, Barry Marshall and Robin Warren were awarded the Nobel Prize for the discovery of *H. pylori*. This year, similar recognition has been given to Harald zur Hausen for the discovery of HPV, and to Françoise Barré-Sinoussi and Luc Montagnier for the discovery of HIV.

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Further reading

Barré-Sinoussi, F., Chermann, J.C., Rey, F., & others (1983). Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). *Science* **220**, 868–871.

Dürst, M., Gissmann, L., Ikenberg, H. & zur Hausen, H. (1983). A papillomavirus DNA from a cervical carcinoma and its prevalence in cancer biopsy samples from different geographic regions. *Proc Natl Acad Sci U S A* **80**, 3812–3815.

Warren, J.R. & Marshall, B. (1983). Unidentified curved bacilli on gastric epithelium in active chronic gastritis. *Lancet* **i**, 1273–1275.

National Subject Profile for higher education programmes in microbiology

The Higher Education Academy recently launched a landmark series of National Subject Profiles, researched and written by the Academy's Subject Centres. Informed by discipline communities and practitioners, each Profile provides an evidence-based overview of higher education provision in a specific discipline, summarizing the range of learning experiences available and highlighting areas for development. Two Profiles were produced by the HEA Centre for Bioscience – Microbiology and Biochemistry.

Each Profile was managed by a panel comprising representatives from academia, employers, students and learned societies. Sue Assinder (SGM Education Officer) chaired the Microbiology panel and Janet Hurst was a member to represent the various microbiology learned societies. The panel used data in the public domain where this was available (e.g. centrally published by funding councils and the results of the National Student Survey). Where new data were required, the panel was grateful for the help of SGM representatives in several academic departments who provided information about their programmes and also allowed their students to be surveyed about their learning experiences. The panel also made use of data collected by the SGM, such as the degree programmes followed by winners of SGM undergraduate prizes.

The Profile reviews current provision in relation to the historical development of microbiology as a teaching discipline and its significance for society, for the economy and on research in other biosciences. It details the current range of higher education undergraduate and taught postgraduate programmes, including their curriculum content and the key teaching, learning and assessment patterns. Data are presented on trends in staffing profiles, student entry profiles, student numbers and graduate destinations. There are also some baseline comparisons with other countries, including models of provision elsewhere and transferability of qualifications.

A key message is that students wishing to study microbiology at university are offered programmes that are exciting, relevant and diverse in their approaches to teaching, learning and assessment. The nature of undergraduate provision is very varied, and this enables students to choose a programme that meets their needs in terms of teaching and assessment methods used, support provided, options available and specialisms taught. Although there has been concern in the sector in recent years about the decrease in the number of 'named' microbiology programmes on offer, the Profile shows that large numbers of undergraduate students are still being exposed to a substantial amount of microbiology teaching. Although any loss of 'named' programmes is to be regretted from the perspective of maintaining the profile of the discipline, the Profile provides reassuring data about the number of students graduating with the relevant microbiological knowledge. Data on graduate destinations show that microbiology degrees provide entry to fascinating and varied careers both within and outside the biosciences.

The microbiology students surveyed were generally very positive about their experiences. Most reported that their lecturers were enthusiastic, that their practical and generic skills had been developed effectively and that they would recommend their degree programme to others. They were more negative about aspects flagged nationally as concerns in the annual National Student Survey, such as feedback, career guidance and availability of relevant work experience.

Against this largely positive backdrop, the evidence presented in the Profile highlights important educational and intellectual issues. These include the need for the curriculum to reflect the societal and economic impacts of microbiology and to keep pace with the rapid expansion of knowledge in this field. Alongside this, programmes must meet the needs and support the career aspirations of all students by achieving an appropriate balance between discipline-specific knowledge and transferable skills. And, crucially, students must have adequate opportunities to develop skills in practical microbiology, including wherever possible the availability of laboratory-based final year research projects. These are highlighted as priority areas for future development by the HEA Centre for Bioscience.

Resource issues are also emphasized, including the need for adequate funding per student to support a laboratory-intensive experience and the availability of appropriate teaching space. Attention is also drawn to the tensions often faced by academic staff when dividing their time between research and teaching, and the recognition of the latter as an appropriate career option.

Those involved in producing the Microbiology Profile hope that it will be a useful reference for both academics and students, together with a wide range of other groups such as employers, careers advisors and prospective applicants. It is a starting point for discussion about how university microbiology programmes can best meet the needs of both students and employers and ensure a continued flow of microbiology graduates that is commensurate with the demands of the UK economy. It gives academic departments information from which to reflect on the appropriateness of their own programmes and provides a foundation that can be updated periodically to enable continual enhancement of the student learning experience.

The Microbiology and Biochemistry Profiles can be downloaded from the website of the HEA Centre for Bioscience (www.bioscience.heacademy.ac.uk/events/themes/sled.aspx).

Sue Assinder
SGM Education Officer

conferences

New for **2009**

From 2009, Society meetings will have a new look. The scientific sessions over three and a half days will cover the latest topics in modern microbiology, within a framework of fewer parallel sessions in the mornings, standalone keynote lectures and afternoons packed with workshops, debates, demonstrations and mini-symposia catering for all areas of microbiological science. Poster-viewing will take place over a drink in the evenings. Career development and microbiology education will also be covered. The ever-popular Gala Dinner will retain its Tuesday evening slot.

Divisions

Scientific programmes will be organized by five Divisions:

Prokaryotic Microbiology **Eukaryotic Microbiology**
Virology **Education** **Irish**

Each scientific division is divided into four themes

Microbial diversity and evolution *Fundamental microbiology*
Translational and applied microbiology *Infectious disease*

The Education Division covers all aspects of education, training and career development. The Irish Division holds its own meetings in Ireland, but also contributes to the planning process of the main meetings.

Division members are selected to ensure that the appropriate areas of interest are covered. Elections for vacancies will be held annually. Each division is headed by a Chair and Chair-elect, who sit on the Scientific Meetings Committee responsible for making decisions on policy matters and meetings content. The Scientific Meetings Officer, who also has a Deputy, reports to Council. Society members can also make proposals for sessions to the Scientific Meetings Committee. This organizational matrix is shown below:

	SCIENTIFIC MEETINGS OFFICER & DEPUTY (Hilary Lappin-Scott & Chris Hewitt)				
	Divisions				
	Virology	**Eukaryotic Microbiology**	**Prokaryotic Microbiology**	**Education**	**Irish**
Chair Chair-elect Council rep*	Stuart Siddell Mark Harris David Blackbourn	Geoff Gadd Neil Gow*	Petra Oyston* Ian Henderson	Jo Verran Sue Assinder*	Evelyn Doyle John McGrath Charles Dorman
Themes					
Microbial diversity & evolution	John Walsh John McCauley Tony Fooks	Paul Dyer Saul Purton Tom Richards	Lucinda Hall Mark Osborn Ian Head Malcolm White	David Adams Alan Cann Goura Kudesia Lynne Lawrance Sara Burton Martin Adams	Catherine Adley Conor O'Byrne John Morrissey Gerard Wall Kevin Kavanagh
Fundamental microbiology	Ade Whitehouse Steve Goodbourn Lisa Roberts	Adrian Harwood Al Goldman Mick Tuite	Nick Dorrell Maggie Smith Steve Busby Jeff Green		
Translational microbiology	Martin Cranage Paul Duprex John Doorbar	Geoff Robson Diane Wilkinson Dimitris Charalampopoulos	Peter Andrew Cath Rees Paul Langford Stuart Stocks		
Infectious disease	Judy Breuer Deenan Pillay Katie Jeffery	Alan Fairlamb Michael Ginger Antonio Di Pietro	Mark Stevens Paul Everest Dietrich Mack Adam Cunningham		

Spring**09** | Harrogate International Centre
www.sgmharrogate2009.org.uk

30 March–2 April 2009

Legacy of Fleming – Diagnosing, preventing, controlling and treating infectious diseases in the modern world

Who should attend?

This will be the largest gathering of microbiologists in the UK in 2009. Attendance is essential for anyone who wants to keep up to date with modern microbial science.

Where is it?

Located in the heart of historic Harrogate, gateway to the Yorkshire Dales, the International Centre has excellent facilities. Harrogate is within easy reach of Leeds, York, Manchester and Newcastle, with convenient rail, air and road transport links.

Grants

Conference grants are available to SGM Associate Postgraduate Student Members.

Deadlines

Abstract submission
5 December 2008

Earlybird registration
27 February 2009

Novel antimicrobials and therapies
Antibiotics and the environment
Impact of medical intervention on microbial evolution
Infection control
New ways of rapid diagnosis
Antibiotics in food preservation
Production, formulation and delivery of antimicrobials (industry session)
Multi-drug resistant TB
Mechanisms of resistance (with BSAC)
Antibiotic resistance in staphylococci
The human microbiota
Microbes in history: war wounds

Virology

The programme will include symposia on *Molecular evolution of virus pathogens*, *Structural insights into virus biology* and *Prions*, 7 workshops (*Pathogenesis* | *Gene expression* | *Immunovirology* | *Epidemiology, evolution and modelling* | *Entry, trafficking and egress* | *Virus structure* | *Plant virology*) and poster sessions.

Other highlights

New SGM Prize Medal – Professor Stanley Prusiner
Careers and Education Workshops
Gala Dinner at the Old Swan Hotel
Trade Exhibition
Prize Lectures
Poster Sessions

Go to **www.sgmharrogate2009.org.uk** for programme details, online registration and abstract submission.

Autumn**09** | Heriot-Watt University Edinburgh

7–10 September 2009

Translational microbiology

The 200th anniversary of the birth of Darwin will be marked by a symposium at this meeting, alongside a range of sessions that explore the many ways that microbes can be put to work, such as in food or drug production, cleaning up the environment, in industry and as model organisms. See www.sgmheriot-watt2009.org.uk for details.

Other**Events**

15th Conference of the Federation of Infection Societies

Cardiff City Hall
2–4 December 2008
www.fis2008.co.uk

4th Annual Recent Independent Virology Researchers' (RIVR) Meeting

Breadsall Priory Hotel, near Derby
5–6 January 2009

For further details, contact Alain Kohl (e Alain.Kohl@ed.ac.uk).

Irish**Division**

22–23 January 2009

Enterobacter sakazakii
University College Dublin, Ireland

Joint organizers: UCD Centre for Food Safety & SGM Irish Division.

23–24 April 2009

Innovative models and systems for studying microbial pathogenesis
University of Cork, Ireland

For further details, contact John Morrissey (e j.morrissey@ucc.ie).

For details of other Irish Division activities, contact Evelyn Doyle (e evelyn.doyle@ucd.ie).

Abstract Book – Dublin meeting

The full text of the abstracts book is available as a PDF on the SGM website.

For up-to-date information on all future Society events:
www.sgm.ac.uk/meetings

Organization

The organization of SGM conference programmes is co-ordinated by the Scientific Meetings Officer, **Professor Hilary Lappin-Scott**, and Deputy Scientific Meetings Officer, **Professor Chris J. Hewitt**. Suggestions for topics for future symposia are always welcome.

The administration is carried out by **Mrs Josiane Dunn** at SGM Headquarters, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (t 0118 988 1805; f 0118 988 5656; e meetings@sgm.ac.uk).

Abstracts

Titles and abstracts for all presentations are required in a standard format and should be submitted through the SGM website by the advertised deadlines. For further information contact the Administrator.

delivering modern microbial science

society for general microbiology
sgmconferences

Nematode-killing fungi

When we think of predatory creatures, it tends to be in terms of tigers stalking other animals in the jungle. But as **Dariel Burdass** describes, fascinating examples of killers and their victims can be found on a much smaller scale. This article explores how certain fungi have adapted, forming lassoes and sticky pads, to capture nematodes for food.

The fungi that have developed ways of utilizing nematodes as their main food source (nematophagus fungi) can be divided into two different groups:

- *endoparasitic fungi* which produce spores that infect nematodes
- *predatory fungi* which catch their prey with specialized hyphal devices

Endoparasitic nematophagus fungi

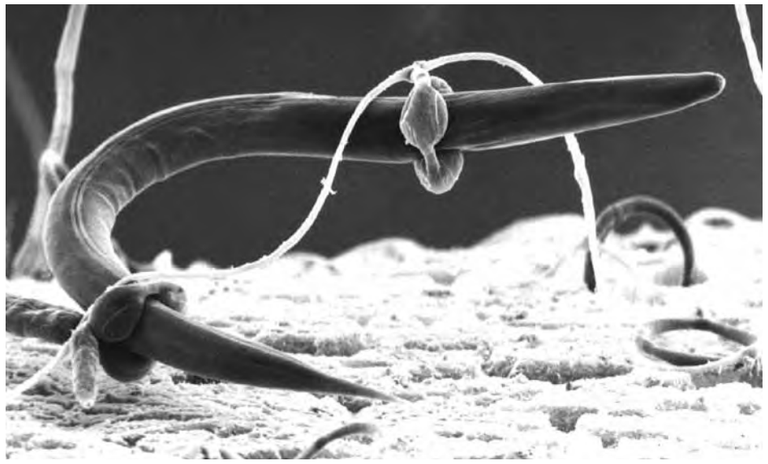
These fungi are obligate parasites, which means that they spend almost all their life cycle inside infected nematodes and only emerge to sexually reproduce, i.e. to develop and disperse their spores. They use the nematode as their main or only food source.

The spores release a chemical which attracts the nematodes towards it (by chemotaxis), as the nematode senses this as potential food. This helps to ensure that attachment takes place. The fungal spores are either directly ingested by the nematode, where they attach to the gut cuticle, or are sticky and adhere to the nematode's external cuticle.

Once attached, the spore germinates, producing a germ tube which penetrates the nematode's cuticle. The fungus grows, creating a network of hyphae that produce enzymes which break down the nematode's insides into a nutritional soup. The nematode dies within 48 hours as a result. 3–10 days after initial infection, the fungus generates aerial hyphae along the length of the cadaver. These break through the cuticle and produce aerial spores which are dispersed by the wind and rain. The process starts all over again. If conditions are not favourable, the fungus can produce resistant spores within the dead nematode that allow it to survive until conditions for growth are suitable.

What are nematodes?

Nematodes are tiny non segmented 'worms'. They are 100–1,000 µm long, which is approximately the width of a human hair. They taper at both ends and are covered by a transparent protective cuticle. They are not related to segmented worms. Nematodes are widespread, occurring in all types of soil, rotten wood and animal dung. Their numbers in a nematode-rich habitat can reach 20 million per m^2. Nematodes cannot see and hunt for food using their sense of smell.



▲ Top. Light micrograph of a nematode captured by the constricting rings of the predatory fungus *Drechslerella anchonia*, showing a germinating spore (conidium) with the germ hypha producing a series of constricting rings around the nematode. *MycoAlbum CD – George Barron*

▲ Bottom. Scanning electron micrograph of a nematode captured by the constricting rings of the predatory fungus *D. anchonia*. *George Barron & Nancy Allin, University of Guelph, Canada*

Predatory nematophagus fungi

Over 200 species of fungi use specialized structures to capture free-living nematodes. They produce traps at intervals along the length of their hyphae that capture, penetrate, kill and digest a nematode's contents. The traps are usually formed in response to the presence of substances produced by the nematodes. Hyphal differentiation occurs spontaneously, usually very quickly, within a few hours, to produce functional structures (traps). The type of trap produced will depend on the fungal species involved. The predatory fungus secretes chemicals that attract the nematode towards it (by chemotaxis), leading quickly to its certain death.

There are two basic type of traps that have evolved separately.

Adhesive traps

Adhesive traps capture their prey by means of an adhesive layer covering all or part of the trap. Although the traps are referred to as sticky, they are not sticky like adhesive tape because the devices don't get clogged up with debris such as soil. Instead the adhesive on the fungal trap binds strongly to sugar compounds on the surface of the nematode.

Different kinds of adhesive trap include:

- ***networks*** – the most common type of trap. They resemble a mesh of interlocking loops which ramify through the soil.
- ***knobs*** – erect stalks with an adhesive bulb at the end that are spaced out along the length of the hyphae.
- ***non-constricting rings*** – composed of 3 cells that do not change in size or shape. They always occur alongside adhesive knobs.

Following adhesion, the nematode's fate is sealed. Even if it struggles to break free, the fungal trapping organ, which is firmly bound to the nematode, will break from the hyphae, remaining attached to the nematode and initiate infection.

Constricting rings

This is the most sophisticated of the trapping devices and is common in the species *Drechslerella anchonia* (formerly *Arthrobotrys*). The nematode wriggles into the ring hoping to find food, but as it touches the ring it triggers a response. Three curved cells at the

end of a short stalk, which make up the closed loop, swell rapidly inwards, within 0.1 seconds crushing the worm like a noose around the neck. Death follows very quickly.

Once ensnared, the fungus pierces the nematode's cuticle using a narrow penetration peg, which swells inside the host to form an infection bulb that the hyphae grow from. Fungal enzymes break down the contents of the nematode and the nutrients are translocated elsewhere within the hyphal system for growth or spore production. Growth does not occur at the site of the hyphal trap.

This phase usually takes 1–3 days, before hyphae grow out of the cadaver and sporulate.

Nutrition

Predatory fungi have evolved these trapping devices to obtain nutrients and give them an edge over other types of organisms in habitats where population densities are high and consequently competition for resources is fierce.

The primary function of predatory fungi is wood decay. Wood is mainly composed of carbohydrates: cellulose and lignocellulose. The carbon to nitrogen ratio (C:N) of wood is very high at 300:1–1,000:1 or even higher. For good growth to occur, most organisms require a C:N ratio of 30:1 to produce nucleic acids, proteins and enzymes. For predatory fungi nitrogen is the limiting factor for growth. Nematophagus predatory fungi get their extra nitrogen from digesting the nematode's biomass.

This means that predatory fungi are not true saprotrophs (which live on dead organic matter) as two phases that run in parallel are necessary to supply them with the correct nutrients for growth – the predatory parasitic phase and the saprotrophic phase. Predatory fungi are facultative parasites.

Biological control

Experiments are being carried out to see if predatory fungi can be used to control parasitic nematodes that infect grazing animals such as sheep. These gastrointestinal nematodes can kill their host animal, leading to significant financial loss for the farmer. Treatment is almost exclusively with drugs that kill or expel the worms. However, nematodes are now becoming resistant to the drugs, so scientists are looking at other methods of treatment.

One idea that is being tested is the use of the nematode trapping fungus *Duddingtonia flagrans*. This fungus uses the adhesive net technique to trap and kill nematodes. Researchers are feeding *D. flagrans* to the animal as spores, either directly in their food or in mineral licks. The fungal spores pass through the digestive system of the animal both unharmed and without germinating and are deposited on the grass in the faeces. The spores then germinate producing mycelia with hyphal traps that catch and kill the nematodes. This significantly reduces the number of nematodes on the pastureland that are able to reinfect the grazing animal.

The oyster mushroom

Pleurotus ostreatus, the oyster mushroom, produces a very powerful toxin from special structures on its hyphae. This toxin paralyses the nematode, but doesn't kill it. The fungus then sends out specialized directional hyphae that penetrate the nematode's cuticle and digest the contents.

Dariel Burdass, SGM

Further sources of information

www.pnas.org/content/104/20/8379.full

www.uoguelph.ca/~gbarron/MISC2003/feb03.html

Deacon J.W. (1997). *Modern Mycology*, 3rd edn. Oxford: Blackwell Science.

Jansson, H.-B. & others (1985). Differential adhesion and infection of nematodes by the endoparasitic fungus *Meria coniospora*. *Appl Environ Microbiol* 49, 552–555.

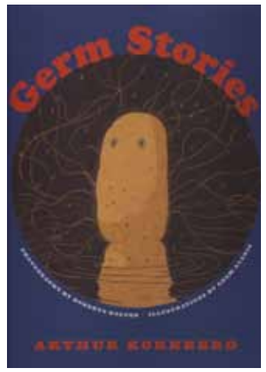
MiSAC Poster Competition 2009 – Microbes and Climate Change

This year SGM is sponsoring the annual competition, which asks school students in two age groups (KS 3 and GCSE) to produce an eye-catching poster to illustrate to their peer group one important aspect of the role of microbes in climate change. There are cash prizes for both the winning schools and students in each category. The closing date for entries is 31 March 2009.

Checkout **www.microbiologyonline.co.uk** for details and to download an entry form or email **education@sgm.ac.uk** for a competition flier and informative factfile about this subject.

Book review

Germ Stories



A. Kornberg
University Science Books
(2007)
£17.99 pp. 72
ISBN 978-1-891389-51-1

Hurry, hurry to the parade
Of the strangest creatures
ever made.
No legs, no fins, no mouths,
no eyes,
Little beasties of the tiniest
size

Germ Stories is a charming anthology of microbiological verse. Written by the Nobel laureate Arthur Kornberg, it comprises 12 poems about bugs, both good and bad, beautiful and ugly. Originally intended as bedtime stories for his children, they have been updated for his grandchildren (and the 21st century) to include microbes such as HIV and *Helicobacter pylori*.

This book is both educational and highly entertaining. The rhyming couplets are interspersed with Roberto Kolter's fascinating photographs and accompanying explanatory text. The lyrical quality of Kornberg's writing is complemented by Adam Alanz's enchanting illustrations which strike a careful balance between the whimsical and the scientifically accurate.

My only criticism would be that, considering its intended audience, some of the terminology is advanced. I doubt words like 'microbiocide', 'ATP' and 'antitoxin' normally feature in the average child's bedtime tales (unless your Dad happened to win a Nobel prize in Medicine!), but the fluidity of his language fully compensates for this. It would certainly suit the inner child lurking in an adult biologist and what better way to teach your children the important, yet difficult, concepts of food hygiene, antibiotic resistance and vaccination?

This is one of those tactile books that will survive the digital age. A hardback with huge, colourful images and thick, glossy pages, it invites you to snuggle up with it under a warm duvet or next to an open fire. It is a book to be treasured and would make an ideal Christmas present, for the young or old.

Gemma Sims, SGM

SGM at ASE Annual Conference 2009

8–10 January, University of Reading

SGM and the Microbiology in Schools Advisory Committee are joining forces to promote microbiology at the Association for Science Education's flagship event.

Not only can teachers visit us on Stand CS31 in the Exhibition, to see our latest multimedia resource for KS3 and GCSE *Microbes: the Good, Bad and Ugly*, but they can also hone their practical skills at our drop-in workshop. This will take place in a lab in the AMS Building, shared with prestigious safety body CLEAPSS.

Under the banner *Hands-on Practical Microbiology for the new GCSEs*, experts from MiSAC will demonstrate some essential methods which delegates can try out under their professional guidance. In addition there will be workstations with some simple but effective practical investigations to see.

Biology in the Real World: Bringing the Curriculum to Life

9 January 2009
Room 109, Palmer Building, University of Reading

SGM and MiSAC are also sponsoring a speaker on TB vaccines in this one-day symposium, which is organized by members of NUCLEUS.

Dr Helen Fletcher, a senior postdoctoral scientist at the Nuffield Department of Clinical Medicine, Oxford, will answer the question *Why do we need a new vaccine for tuberculosis?* With 2 million deaths a year from TB and an estimated third of the world's population infected with *Mycobacterium tuberculosis*, new vaccines for TB are urgently needed. Drug treatment and the BCG vaccine have failed to control the current epidemic. Dr Fletcher will talk about MVA85A, a new vaccine designed to boost the protective immune response induced by BCG, and discuss the scientific, clinical and ethical issues surrounding the development of new TB vaccines.

The topic will be of particular interest to teachers of KS4 and post-16 biology as factual and ethical issues relating to TB and vaccination figure large in the specifications.

See **www.ase.org.uk** for further details of all events at the Annual Conference.

Please note that anyone wishing to attend any event at the conference must register, either beforehand or on-site.

Gradline aims to inform and entertain members in the early stages of their career in microbiology. If you have any news or stories, or would like to see any topics featured, contact **Jane Westwell** (**e** j.westwell@sgm.ac.uk).

A Concordat to support the career development of researchers

Tristram Hooley and **Tennie Videler** from Vitae, look at the new Concordat and ask what it will mean in practice for research staff and PIs.

What is Vitae?

Vitae (www.vitae.ac.uk) is a national organization championing the professional and career development of researchers. Funded by Research Councils UK (RCUK) and managed by CRAC: The Career Development Organization, Vitae builds on previous work by the UK GRAD Programme and UKHERD to involve all stakeholders in supporting the professional development of researchers. Through national activities, and the work of eight regional Hubs, Vitae works with higher education institutions, researchers and employers for real and positive change.

Vitae's vision is for the UK to be world-class in supporting the professional development of researchers and researcher careers.

The programme has four key aims:

- Championing the development and implementation of effective policy
- Enhancing higher education provision through sharing practice and resources
- Providing access to development opportunities and resources
- Building an evidence base to support the researcher development agenda

As a researcher or manager of researchers, Vitae offers you access to a range of information and services that can support your work; visit the Vitae website to find out more. The website includes dedicated sections dealing with professional development and careers for research staff. We also offer a regular newsletter for supervisors and managers of research and regular events and courses to help you get to grips with issues and access a network of colleagues with whom you can share ideas and practice.

The Concordat

The 2008 Concordat to support the career development of researchers was launched in June. It is a statement of key principles for the support and management of researchers and their careers, agreed by Universities UK and major funders of research in the UK. It recognizes that permanent research or academic positions are limited. The Concordat could deliver real progress but its success depends on researchers and their managers re-examining the ways they work.

The Concordat's key principles are:

1 Recognition of the importance of recruiting, selecting and retaining researchers with the highest potential to achieve excellence in research.

2 Researchers are recognized and valued by their employing organization as an essential part of their organization's human resources and a key component of their overall strategy to develop and deliver world-class research.

3 Researchers are equipped and supported to be adaptable and flexible in an increasingly diverse, mobile, global research environment.

4 The importance of researchers' personal and career development, and lifelong learning, is clearly recognized and promoted at all stages of their career.

5 Individual researchers share the responsibility for and need to proactively engage in their own personal and career development, and lifelong learning.

6 Diversity and equality must be promoted in all aspects of the recruitment and career management of researchers.

7 The sector and all stakeholders will undertake regular and collective reviews of their progress in strengthening the attractiveness and sustainability of research careers in the UK.

What will the Concordat achieve?

The Concordat encourages institutions to embed support for researchers and maximize their potential both within research roles and beyond. Managers of researchers (such as PIs) are encouraged to look for opportunities to develop their staff by mentoring them and giving them more responsibilities. Typically this might be done through appraisals, professional development courses and access to tailored advice.

Personal developmental activity often impacts the success of projects; it can increase the effectiveness of researchers and help keep motivation and vision within a longer term career context.

Commitment to professional development also has to be personal. Researchers should take control of their development and make the most of appropriate opportunities offered by their employers.

Practical ideas for implementation of the Concordat for research staff:

- See if you can join a mentoring scheme, either as a mentor or a mentee
- Be proactive about networking
- Are you represented? Could you join a committee in your institution or a postdoctoral or similar society?
- Discuss your career and development in an appraisal with your line manager
- Explore your career options with a careers advisor. Many institutions now have one specializing in research staff
- Attend appropriate transferable skills training courses
- Consider how your current skills could be translated to other careers

You can find out more about the Concordat and related developments by visiting the Vitae website at **www.vitae.ac.uk/policy-practice/**

Tristram Hooley
Senior Manager, Stakeholders and Networks, Vitae (**e** tristram.hooley@vitae.ac.uk)

Tennie Videler
Programme Manager, Researchers (**e** tennie.videler@vitae.ac.uk)

SGM Meeting at Harrogate, Spring 2009

Workshop for early career microbiologists – Personality at work

1915, Monday 30 March 2009

Delivered by Sarah Blackford (Society for Experimental Biology)

Have you ever wondered why there are some people you get on with and others you don't? Why it is that some people just don't seem to be thinking along the same wavelength as you or seem disorganized or dispassionate?

In this session, you will learn about a well-known personality inventory, the MBTI (Myers Briggs Type Indicator), and how it can help to decipher between different personality types. The session will give you the opportunity to recognize some of the personality elements which describe you or that you recognize in your friends or colleagues and will attempt to demonstrate the importance of considering personality in your day-to-day working life and for your career development and planning. As well as being informative, the session will take a light-hearted and interactive approach giving you the insights as well as the practical uses for this fascinating instrument.

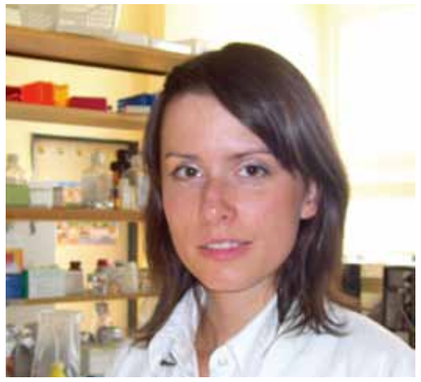
Sarah Blackford is the Education & Public Affairs Officer for the Society for Experimental Biology, SEB (www.sebiology.org). With an early background in biological sciences research and publishing, she is now a qualified careers coach and has worked as a careers consultant within university careers services and, more recently, with the SEB for over 10 years. Sarah is a qualified MBTI (Myers Briggs Type Indicator) practitioner and uses it as a basis for self-awareness in the career development programmes she runs which are specifically designed for postgraduates and postdoctorals.

The session will be followed by buffet and drinks.

This event is restricted to postgraduate students and first postdocs attending the conference and pre-registration is essential.

Enhancing the undergraduate experience

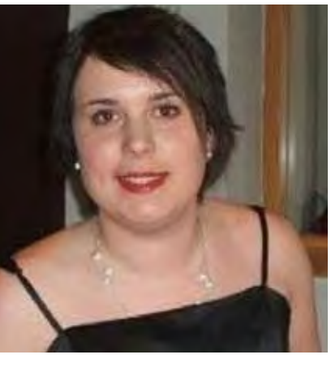
Each year, the SGM Vacation Studentship scheme funds more than 40 undergraduate research projects lasting 6–8 weeks during the summer before the students enter their final year. Summer students gain valuable practical experience and an insight to microbiology research. **Jane Westwell** caught up with three students from the 2007 cohort.



Li Yen Mah – University of Manchester
(supervised by Dr Christian Heintzen)

Li Yen's project looked at VVD – a photoreceptor and repressor of light-signalling in the model eukaryotic microbe *Neurospora crassa* that also plays a role in modulating light-resetting of the organism's circadian clock. The aim of her project was to identify domains within VVD that are important for resetting of the circadian clockwork. After the project Li Yen commented, '*I am very inspired by Dr Heintzen's and his team's hard work, and this experience has instilled in me the passion to pursue a career in scientific research.*'

Li Yen has been accepted by the Beatson Institute of Cancer Research in Glasgow to pursue a PhD studying how autophagy is regulated, and how this might integrate with apoptosis to cause tumour cell death. Her long-term aim is to be a principal investigator in a university.



Leanne Allum – Cardiff University
(supervised by Professor Lynn Boddy)

Leanne's project focused on investigating isolates of the endangered oak polypore *Piptoporus quercinus* for evidence of inbreeding. Samples came from different areas of Windsor Great Park, Germany and Wales and early results from Leanne's project indicated that the species may be highly inbred. Before the project started Leanne hadn't been sure that a career in science was for her but afterwards she observed, '*The placement definitely made me want to continue working in labs as I loved the hands on experience.*' Leanne was pleased to graduate with an upper second class honours degree and aims to find a lab-based role near her home in Wiltshire.

Anna Janowicz – University of Glasgow
(supervised by Dr Robert Davies)

Anna studied two different ethanol-producing micro-organisms – *Zymomonas mobilis* and *Saccharomyces cerevisiae*, determining which one would be most suitable for large-scale bioethanol production. Anna enjoyed the opportunity to learn much more about real-life research work than during routine laboratory classes. She found the studentship good preparation for her industrial placement at the University of South Bohemia in the Czech Republic which started a month after she completed the studentship. Anna commented, '*I think that all students of biological sciences should have an opportunity like this to find out what real research is like and whether it is a good choice for them or not. It reassured me that this is something I want to do in future. It also provided a good insight into what to do if things go awry, which is a helpful experience regardless of what field you go into!*'

Anna returned to Glasgow recently to complete her MSc. She plans to apply for a position as a trainee clinical microbiologist and continue research in this field with a view to one day leading her own research team.

council**08–09**

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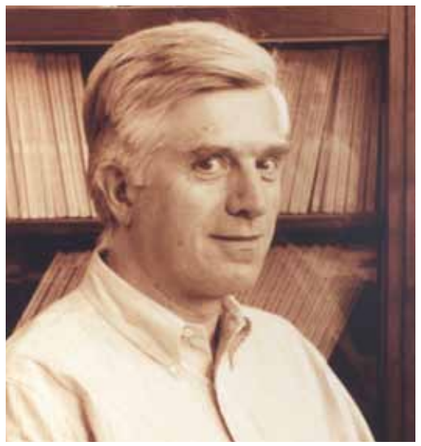
Professor Chris Thurston

(29.06.**1944**–18.07.**2008**)



Chris Thurston died after a long illness at the Royal Hospital for Neuro-disability in London. He had suffered profound brain damage following a major heart attack 8 years ago and remained in care for almost all this time. Chris was a polymath, an adventurous and successful researcher and an accomplished teacher, administrator and communicator. During his academic career, conducted almost entirely in the University of London Colleges, he played a major role in the development of microbiology and higher education in London. Chris always made a big impression: he was unusually articulate, humorous and generous.

Chris was a London microbiologist through and through, but not a Londoner by birth. Born in Norfolk, he went to King Edward VI School in Norwich, where he was Head of House, and active in school rowing, drama and the choir. Chris was also a Norwich Cathedral chorister. After his arrival in University College London (UCL) as an undergraduate, Chris never left the capital to work, apart from a sabbatical period (1979–80) with Bob Schmidt at the Virginia Polytechnic Institute, Blacksburg, USA.

Chris had entered UCL to read microbiology, but in the Department of Botany. Microbiology departments were very thin on the ground, so Chris obtained his degree under a hybrid scheme jointly administered by UCL and Queen Elizabeth College London (QEC), where microbiology was well established. Chris stayed at UCL to do a PhD on the alga *Chlorella fusca* under the supervision of Philip Syrett. When Syrett was appointed to a chair at Swansea, Ian Morris acted as supervisor.

It may seem extraordinary to 21st century young scientists that, while still working for a PhD, Chris was appointed in 1969 to the first lectureship in Biochemistry at QEC in leafy (and trendy) Kensington. In 1970, having obtained his PhD, he transferred to the Microbiology Department, an influential, vigorous and congenial consortium. The Department was established in 1961 from a Bacteriology Department that had existed since 1914. At the time of Chris's move there, the Department comprised John Pirt (the only Professor and Head of Department), together with 'Simos' Anagnostopoulos, Brian Bainbridge, Michael Bazin, Don Kelly, Ted Mathison and Tony Trinci. (Shortly after, in 1975, this author joined to replace Don Kelly). Of these lecturers, six became university professors – remarkable then, less remarkable now. Equally remarkable was the peripatetic electric typewriter that was used by all staff except John Pirt, who had both typewriter and a secretary to use it. It was certainly not remarkable to be appointed to a permanent academic position without a PhD; indeed, Chris took the place of Mr John Birch in John Pirt's group, and Brian Bainbridge, Don Kelly and Tony Trinci were all appointed before award of their PhDs. Nevertheless, PhD or not, Chris made quite an impression as an extremely bright yet sociable new colleague at QEC.

One of the defining characteristics of Chris's research career was his enthusiasm for tackling technically and intellectually difficult projects. Those topics would be challenging now, but truly daunting in the 1970s and 1980s. Chris stuck with the intransigent *C. fusca* for over 15 years. However, for most of the 1980s, he became fascinated by another, apparently unrelated, line of research on the design and fabrication of redox-mediated electrochemical sensors using whole micro-organisms. In collaboration with Peter Bennetto (Chemistry Department), Jeremy Mason, John Stirling (Biochemistry), Sibel Roller and Gerard Delaney, over a dozen papers, chapters and patents were generated. The two most cited (Roller *et al.,* 1984, *J Chem Tech Biotechnol* **134B**, 3–12; Delaney *et al.*, ibid. 13–27; 79 and 90 citations, respectively) quantify the reduction by diverse bacteria of dyes and show how an appropriate combination of microbe, mediator dye and oxidizable substrate can generate significant, anodic electrode potentials. Subsequent papers described electrochemical bioreactors for treatment of carbohydrate wastes and effluents and application of the principle to biosensors and a sucrose fuel cell to achieve efficient biomass conversions.

Throughout, the science was the motivating force for Chris, but he wanted to share the excitement too and so took great pains to explain his work to others – at home, over the snooker table and to his many colleagues and friends. Equally, he was an excellent listener and always curious to learn what others were doing and how they were doing it.

In 1992, he published his first paper on the molecular genetics of the commercial mushroom, *Agaricus bisporus*, launching the most productive and highly cited era of his tragically short career. In collaboration with excellent post-doctoral researchers and his long-standing friend David Wood (HRI) and funded by competitive research council grants, Chris tackled the cloning and characterization of genes encoding proteins involved in the degradation of cellulose, a process critical to the commercial production of the mush-room. Laccase (polyphenol oxidase) received the most attention since it is an abundant glycoprotein that constitutes 2% of mycelial protein during vegetative growth. Chris also published significant papers on *A. bisporus* proteinases, xylan-ase and peroxidases and, in particular, the cellulases that enable growth on crystalline cellulose as carbon source; four cellulose-growth specific (*cel*) genes were isolated and charac-terized and their regulation elucidated. These papers (e.g. Yagüe *et al.*, 1997, *Microbiology* **143**, 239–244; Smith *et al.*, 1998, *Microbiology* **144**, 1063–1069) illustrate beautifully Chris's concise and precise writing and a clarity of thought and expression. This topic occupied Chris until his illness, generating en route his most highly cited paper, a valuable review in *Microbiology* (Thurston, 1994, **140**, 19–26; 578 citations to date). It is quite typical of Chris's modesty that this review acknowledges David Wood as follows: '*…from whom I have learned greatly about laccases and other fungal enzymes; he is not however responsible for any errors or omissions – they simply reflect my imperfect learning*'.

Chris served the SGM with dedication and distinction. He was for many years (1987–92) an Editor of the *Journal of General Microbiology* (the predecessor of *Microbiology*) and served as Professional Affairs Officer (1993–98).

His inclination to incisive thought and reasoning and his love of precise measurements and instrumentation were reflected in Chris's many other interests. He greatly admired optically and mechanically fine cameras and we enjoyed many long debates on the relative merits of rangefinder, large format and SLR cameras. I suspect that Chris would not have objected to the assertion that he treasured the photographic apparatus as much as the images. He appreciated fine Eastern carpets, wines, whiskies (and was a founding member of the exclusive QEC Malt Whisky Society), cigars (for a while) and food (offering, for example, a postdoctoral colleague a dinner party recipe for watercress, date and orange salad). In these worldly pleasures, as in his published research output, Chris valued quality over quantity. At lunchtimes, in QEC days, he would walk through the lanes of Holland Park adjacent to the College, discussing work, life and experiments with a few close colleagues. Chris had a rare regard for an appropriate work/life balance.

Chris was humorous, a mine of information and an observer of small detail. He loved *The Times* crosswords. Chris also had style. In a decade where many of his colleagues paraded dubious sartorial taste (and I dare not mention by name which colleagues), Chris favoured highly polished, brown brogue shoes and tailored, crisp shirts, and his trademark, reddish hair was always well cut and brushed. With his wife Sue, and later their daughter Anna, they lived in beautifully restored period houses. His office at QEC was very organized; neat examples of his curious, rather spidery handwriting were carefully filed.

In the College community, Chris will probably be best remembered for his outstanding contributions to College management through services to at least 20 Committees and Boards during his 31 years at QEC/King's. In 1975–76, he represented the Academic Board of QEC on the College Council, and was later a major driving force in the University of London Board of Studies. He was instrumental in some of the most tumultuous mergers and reorganizations the University has seen. He was a member of the joint Working Party for the merger of QEC, Chelsea College and King's College (1983–85) and played a similar role from 1994 on the Academic Planning Team for the King's/UMDS merger. He was Deputy Head of the Division of Biosphere Sciences from 1988 to 1991 and retained a high profile in Divisional management in its successor, Life Sciences. He worked tirelessly with Marian Simmonds on 'The Cornwall House Project' to plan and bring to fruition the move of the Kensington scientists to Waterloo, generating through a PFI the current home of Biomedical and Health Sciences – the Franklin-Wilkins Building. His work for the project planning team involved innumerable plans, measurements, and company representatives, not to mention a great deal of hassle. These were trying times, yet Chris remained incredibly resilient, exuberant and professional in all his dealings. He made trips overseas to inspect laboratories already designed and furnished by tendering companies: a trip to California was memorable for his hotel room, which was accessed by a high walkway – unsuited to his vertigo. Today's Franklin-Wilkins Building on the South Bank is largely based on the scheme that he helped to generate for disposition of the office, social, teaching, library and research space.

Chris was a thorough, systematic teacher and examiner yet with no sense of self-importance. His intellect never got in the way. Keith Gull remembers Chris accepting with good grace a prank involving the removal of his office door (yes, the removal of the office door) and hiding it in a basement room for a week!

Chris was, in Sue Thurston's words, curious, kind and contented. He was a fine gentleman and an accomplished scientist. The plethora of his accomplishments endeared him to so many. Their loss and sorrow must be compounded by the nature of his long illness.

| Robert Poole, The University of Sheffield

I am very much indebted to Sue Thurston, Keith Gull, Janet Hurst, Joy Poole, Sibel Roller, John Stirling, Tony Trinci and Ann Wood for the recollections, constructive comments and invaluable information received during the writing of this obituary.

hotoffthepress

Science writer **Meriel Jones** takes a look at some recent papers in SGM journals which highlight new and exciting developments in microbiological research.

Getting into shape

Pul, Ü., Lux, B., Wurm, R. & Wagner, R. (2008). Effect of upstream curvature and transcription factors H-NS and LRP on the efficiency of *Escherichia coli* rRNA promoters P1 and P2 – a phasing analysis. *Microbiology* **154**, 2546–2558.

The double helix structure of DNA is one of the great icons of the 20th century. However, DNA has additional structural features. As well as the exact sequence of the nucleotide bases, the shape of the DNA molecule is important. Each comparatively large DNA molecule folds to fit into the cell, but regions remain available for use at a moment's notice, controlled by proteins and DNA structure. The DNA bases ahead of every gene are important for regulating when each is switched on or off by proteins binding at a region called the promoter. DNA curvature and regulatory proteins act together to regulate the efficiency with which genes are used, but many of the exact details are unknown.

Researchers in Düsseldorf, Germany, have been studying how DNA and proteins interact at two promoters in *Escherichia coli*. The P1 and P2 promoters both regulate production of a structural RNA molecule required as part of the protein synthesis machinery. The DNA upstream of P1 is curved, while there is a complete lack of curvature upstream of P2. To test the relative importance of DNA structure and proteins, the researchers changed the DNA bases in the promoter region to vary the amount of curvature. Regardless of curvature, the gene could always be switched on, but the level of activity was highest when the inside of the curved section of DNA and the start of the gene were in the same plane.

Proteins called transcription factors are normally involved in regulating gene activity through modulating interactions with the RNA synthesis system. The researchers went on to test the effect of three *E. coli* transcription factors called H-NS, LRP and FIS in conjunction with the curved DNA molecules. FIS activates P1 promoters while LRP and H-NS inhibit transcription from them. The subtle effects seen with the differently curved molecules differed between P1 and P2, indicating that these two promoters are regulated differently, with P1 being more strongly inhibited.

From these results it is evident that the combined effects of DNA curvature and several transcription factors cause the different levels of activity of each gene, but much more work is needed before accurate predictions can be made for every gene.

Bugs and colon cancer

Allen, T.D., Moore, D.R., Wang, X., Casu, V., May, R., Lerner, M.R., Houchen, C., Brackett, D.J. & Huycke, M.M. (2008). Dichotomous metabolism in *Enterococcus faecalis* induced by haematin starvation modulates colonic gene expression. *J Med Microbiol* **57**, 1193–1204.

The colon is home to around 10^{11} bacteria per gram of contents. For many years, scientists have argued about whether the presence of this vast microbial horde is always in the best interests of its human host. Specifically, the idea that some bacteria are involved in sporadic colorectal cancer has been around, but unproven, for decades. The major difficulties with making any progress are that most of the microbes have not been identified and the interaction between bacteria and the surface of the colon has many unknown features.

To make progress, scientists in Oklahoma, USA, have concentrated on bacteria that are known to damage DNA since this could start the genetic changes required for cancer. The damage is caused by highly reactive forms of oxygen known as superoxide, hydroxyl radicals and hydrogen peroxide which diffuse from some bacteria when they are stressed and into the surrounding animal or human tissues.

The authors have been experimenting with *Enterococcus faecalis*, a minor inhabitant of the colon but one that can cause DNA damage and promote chromosomal instability by releasing reactive oxygen species. They wanted to know how the colon responded to this threat. They have discovered that, although the colon tissue looks perfectly normal under the microscope, the activity of several genes altered rapidly once the bacteria released oxidizing chemicals. Looking in more detail, the researchers proved that *E. faecalis* could activate the NF-κB signalling pathway in white blood cells – this signal can promote tumours.

After checking 5,000 genes, the researchers identified 42 that increased or decreased in expression. Several were involved in the immune response, while 9 were implicated in stress responses and a further 10 in control of whether the cell should divide or die. Looking into the roles of these genes in more detail brought out the message that *E. faecalis* affects a single response network that contains NF-κB signalling and several genes that have been implicated in cancer biology.

The argument about the role of bacteria in colon cancer has thus moved forward with implication of specific mechanisms through which *E. faecalis* can increase the susceptibility of colon cells to DNA damage.

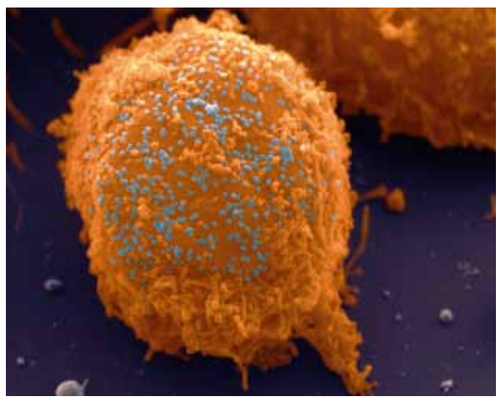
Novel bone disease mycobacterium

Bang, D., Herlin, T., Stegger, M., Andersen, A.B., Torkko, P., Tortoli, E. & Thomsen, V.O. (2008). *Mycobacterium arosiense* sp. nov., a slowly growing, scotochromogenic species causing osteomyelitis in an immunocompromised child. *Int J Syst Evol Microbiol* **58**, 2398–2402.

The most well known *Mycobacterium* species is *M. tuberculosis*, infections of which can result in the disease tuberculosis. Closely related species that cause different, rarer diseases can now be distinguished using molecular genetic and chemical analyses. Several have been identified as the cause of infections in children's bones, although most of these infections have fortunately not been severe. However, treatments with antibiotics to kill the bacteria are quite prolonged and the disease can recur. One recent serious infection in a 7-year-old girl, who had inherited a problem with her immune system, was caused by what turned out to be a novel species of bacteria. She responded well to therapy with a mixture of antibiotics for over a year, with no signs of recurrence of the infection after a further 18 months. However, she probably remains at life-long risk from non-tuberculous mycobacteria.

Staff working at the International Reference Laboratory of Mycobacteriology and National Center for Antimicrobials and Infection Control at Copenhagen in Denmark, along with colleagues at other laboratories in Denmark, Finland and Italy, studied the bacteria in detail because their features did not correspond exactly to any known species. The yellow-coloured bacterial cells grew slowly and looked like typical clinically significant mycobacteria under the microscope. However, more detailed tests that recorded the sequence of several genes from the bacteria showed some differences from all known species. In addition, some results from growth on various laboratory media and an analysis of the fatty and mycolic acids from the cells matched with several different species.

Putting all the information together, the researchers have convincing evidence for a new species that is closely related to *M. intracellulare*, but very clearly different from it. They have named it *M. arosiense* after the Latin name of Aarhus, the city in Denmark where it was first identified.



▲ Coloured scanning electron micrograph of a T-cell (orange) infected with HIV viruses (blue). *Eye of Science / Science Photo Library*

HIV by numbers

Hogue, I.B., Bajaria, S.H., Fallert, B.A., Qin, S., Reinhart, T.A. & Kirscher, D.E. (2008). The dual role of dendritic cells in the immune response to human immunodeficiency virus type 1 infection. *J Gen Virol* **89**, 2228–2239.

Trying to understand exactly why HIV-1 invariably causes a lethal infection has highlighted our lack of understanding of many of the complex interactions in the human immune system. Cells have dual roles, as targets for disruption by HIV-1 and as essential components in an immune response to counter the infection. Hogue *et al.* have tried a new approach to this problem by creating a mathematical model to describe how HIV-1 and cells interact in a human lymph node.

In the decades since HIV-1 was identified, much data have been recorded on how the numbers of viral particles and different types of human cells change throughout an infection. Myeloid dendritic cells (DCs) in the lymph nodes activate T-cells to defend against HIV-1. One type of T-cell, CD8+, has the main protective role against HIV-1 infections through killing infected cells and releasing antiviral factors. Another T-cell type, CD4+, is also important in the body's defences, but is attacked by the virus. DCs can thus promote immunity as a link between the virus and T-cell defences, but are also used by HIV-1 to boost infection. It is difficult to study DCs directly because they reside within lymph nodes which cannot be examined easily. The advantage of a mathematical model in this situation is that it may predict factors that govern the infection and which are easier to test experimentally.

In the first few weeks of infection there is usually a large amount of virus in the body and substantial immune system activity. This stabilizes into a long-term chronic infection that can last years, characterized by much lower numbers of virus particles. Eventually, for unknown reasons, this stable state breaks down, CD4+ cell counts decrease, the levels of virus increase, and the patient experiences the debilitating symptoms of AIDS. All the mechanisms proposed for this change imply that DCs are of key importance, but for several different reasons.

The equations were designed using information from human patients and similar immunodeficiency viral infections in primates. The idea was to have terms for documented significant interactions between HIV-1, DCs, CD4+ and CD8+, concentrating on DCs. The model was good at simulating the numbers of each type of cell in a healthy human lymph node, and in showing how HIV-1 infection results in T-cell depletion. Using mathematical methods for uncertainty and sensitivity analysis allowed the testing of different hypotheses about the roles of DCs. The way that DCs simultaneously infect and alert CD4+ cells seemed to be crucial in establishing infection. Later on, failure of proper DC function has a greater effect on pathogenesis of the disease than the loss of CD4+. One practical outcome of this modelling is to suggest that treatments that improve DC functions could be valuable in improving the outcome of HIV-1 infections.

Science, media & making your point: SGM media training

There are many ways of publicizing research and informing people about microbiology. Talking to the media is one and **Lucy Goodchild** shows that with the right training, this can be a positive experience.

When I ask scientists if they will speak to the media, I am sometimes met with a negative response. '*No way, they'll get my science wrong/misquote me/interview me like Jeremy Paxman would.*' So what is the reality of science in the media and how can scientists make sure they are treated and represented fairly?

To get the right idea, on Monday 7 July 2008, six scientists with specialist areas ranging from HIV research on primates to investigating plankton that produce DMS in the ocean came along to Marlborough House for media training. The tutor, **Myc Riggulsford** from the Walnut Bureau, provided some valuable insights into the minds of the media and helped the participants overcome their reservations about speaking to journalists and publicizing their research.

These days, research councils make public engagement a condition of their funding and many people think scientists have a responsibility to communicate their research, particularly if they have been publicly funded. A great way to do this is to promote their science to the media. This can be done in all sorts of ways, from distributing a press release to organizing a TV or radio interview.

Although every researcher will have a press officer, either working for their research institute or for an organization like the SGM, understanding how the media works will certainly help the scientist get more involved in the process and feel more comfortable speaking to journalists. '*The value of understanding the way the media machine functions is key to providing an accurate and yet wide-reaching portrayal of our research*', said **Dr Jack Gilbert** from Plymouth Marine Laboratory. '*This is increasingly important in light of the need to engage the public more completely in our current output and design of future work.*'

Science journalists often have a background in science. Although they might not all be microbiologists (but some are!), they are able to understand scientific concepts much more than they are given credit for. The vast majority of scientific reporting is responsible and accurate, and journalists do their best to check facts and get comments from experts. The scientist's role in this process is twofold: to supply the media with useful material on which to base stories, and to comment on other people's research.

When presenting science (or anything else for that matter) to the print media, reading age must be considered. Believe it or not, all the content in a broadsheet newspaper is aimed at a reading age of 12–13. So language should be kept simple and scientific concepts should be explained clearly. The same goes for radio and TV interviews – talk to the interviewer as if you were talking to a non-scientist friend at the pub. A minute of jargon and acronyms on the radio is not very entertaining! This doesn't mean you have to compromise your scientific accuracy, you just have to make the research accessible and understandable. '*Science concepts may*

Photos.com / Jupiter

be difficult to explain to the public in some cases, but big fancy words do not help science communication', said **Dr Ernest Asilonu** from Genzyme Ltd.

If you are asked to comment on somebody else's research, or on an emerging news story, the key is speed. Journalists work to exceptionally tight deadlines and will usually need feedback within minutes rather than days. They are often after 'soundbites', short quotes that can be added to a story to give it a different perspective.

At the SGM we get lots of calls from reporters asking to be put in touch with an expert. When this happens, I search our experts database to find people who are happy to speak to the media. As an SGM expert, there are plenty of opportunities for you to get involved with microbiology in the media. We publicize research presented at our meetings, as well as findings published in our four journals. We produce two podcasts, *Micropod* and *Microbe Talk*, which include interviews with specialists on a diverse range of topics, from astrobiology to STIs. And finally, there are opportunities to respond to consultations and review books. If you would like to be added to our database, or would like more information, please email **press@sgm.ac.uk**

The training included tips on how to write a news story, information about how newspapers work, what to wear on TV and even some practice radio interviews. The participants found the day very helpful and are already making use of what they learnt. **Dr Mike Dempsey** from Manchester Metropolitan University is using the techniques for writing abstracts. '*The main message I took from the training was to make sure the key point is in the first sentence.*' This is also a great help for press officers, who look for potential stories by searching through abstracts.

Clinical scientist **Dr Siobhan O'Shea** from St Thomas' Hospital Trust said, '*the main message for me was that dealing with the media does not have to be 'scary' and instead of avoiding it we should be more ready to embrace it as a means of getting science out there to the public. At the end of the training I felt significantly more confident in terms of dealing with the media. As scientists, we are trained to write and give presentations in a particular style which is not appropriate outside the confines of our scientific environment. In terms of the future, the knowledge gained from the training has given me the skills, I hope, to interact more confidently and positively with the media.*'

Professor Martin Cranage from St George's, University of London said, '*the media training day was great and I guess the main point that I took home was get your message over cogently even if it means responding to an oblique question with the answer that you want to give rather than where the interviewer may be trying to take you. The knowledge gained from the training has definitely increased my confidence in engaging with the media.*'

SGM will be running media training events annually, so if you would like to be invited to the next one, please email Lucy at **l.goodchild@sgm.ac.uk**

New media update

Microbe Talk – www.sgm.ac.uk/news/poscast.cfm

In the September episode **Dr Louis Magnarelli**, Director of The Connecticut Agricultural Experiment Station in the USA, talks to us about diagnosing West Nile virus.

A new test for West Nile virus in horses that could be modified for use with humans and wildlife may help track the spread of the disease, according to an article in the September issue of the *Journal of Medical Microbiology*.

New launch for micropod – www.micropodonline.com/podcast.html

Episode 10 has arrived! This month we have a special bumper launch edition of micropod for you. Not only do we have a fabulous new jingle, but we're also twice the length of the normal podcast! But don't worry, it's not just twice as much Lucy and Lucy, it's more interviews, news and two topics.... yes TWO topics!

We're talking (and listening to) music with an interview with **Dr Carl Winter** and his amazing food safety songs.

We also talk about genetic modification, Lucy G interviews **Dr John Heritage** and finds out exactly what GM means. Then Lucy H has a chat with **Professor Nigel Poole** about the media and GM and his experiences of getting genetically modified tomatoes onto supermarket shelves.

SGM now has groups on Facebook and MySpace!

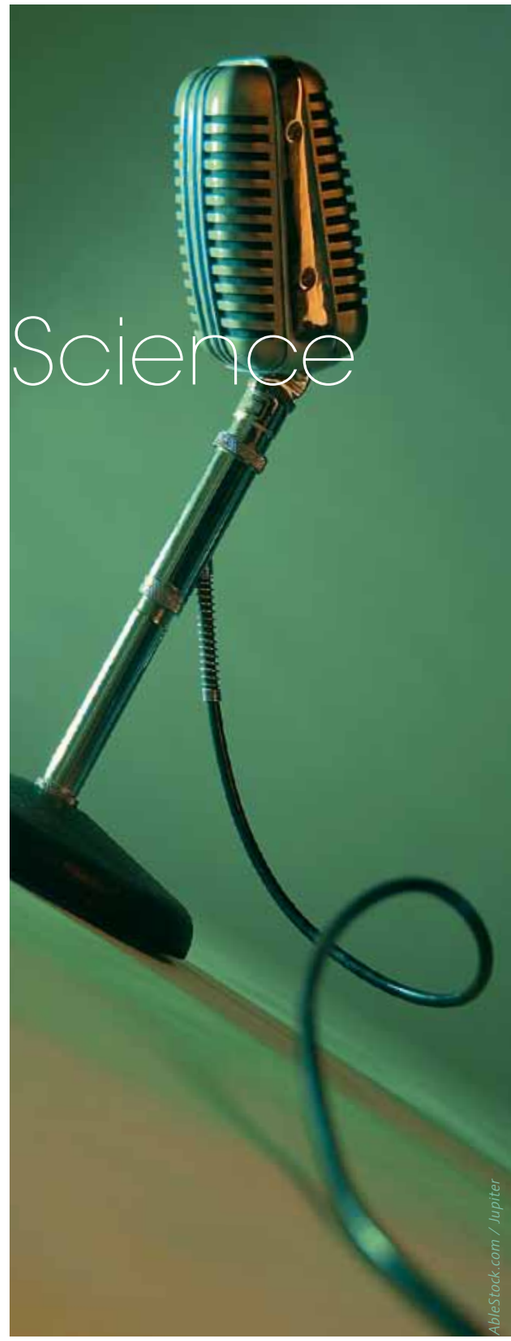
Join in for news about the Society and event updates, as well as discussions and interesting microbiology stories!

Facebook page – www.new.facebook.com/groups/create.php?customize&gid=27768262231#/group.php?gid=27768262231

MySpace page – http://groups.myspace.com/SocGenMicro

SGM likes to encourage the personal developments of early career microbiologists. By supporting the activities of Sense about Science, our members can attend their workshops. **Sarah Maddocks** went on one.

Standing up for Science media workshop



Sense about Science, a charitable trust that counters misrepresentation of science in the media (www.senseaboutscience.org.uk), recently ran a workshop aimed at early career scientists inviting them to *Stand up for Science*. Co-ordinated by the Voice of Young Science network (VoYS), this workshop introduced PhD students and postdocs from a range of disciplines, to the media and confronted the related issues facing scientists today.

Held at the Institute of Biology headquarters in London, the workshop began by introducing *Science and the Media*. Groups of participants discussed the changing roles and image of science and scientists in the public domain. Case studies where science had been misrepresented were offered and discussed with a panel of scientists who were experts in their field, with prior experience of media interaction.

Then science in the media was covered from a reporter's point of view with lively debate from a panel of journalists (*Daily Mirror*, BBC radio and *The Times*). The panel explained how they approach scientific stories and the importance of balancing news and entertainment with conveying science. This made participants appreciate the importance of good communication between the scientific community and the media.

The day rounded off with a 'nuts and bolts' discussion in which members of the VoYS offered practical advice on getting your voice heard in scientific debates including the difficulties involved, areas of misunderstanding and ensuring that 'good' science is communicated to the public.

Having no prior involvement with the media and viewing it with some pessimism, the Sense about Science workshop has helped me to develop a more informed attitude. I appreciate the importance of the media in conveying science to the public and the role that scientists can play in this to ensure that accurate information is published. This workshop would be advantageous for all scientific researchers, regardless of their experience, who want to stand up for science and eliminate its misrepresentation.

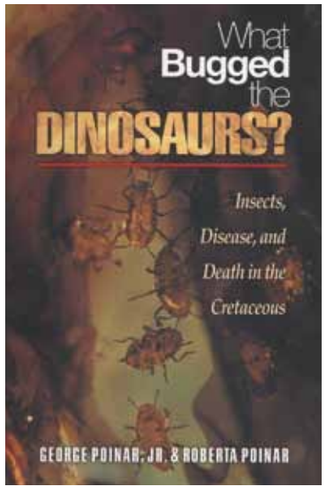
Sarah Maddocks, University of Bristol

reviews

If you would like your name to be added to our database of book reviewers, please complete the book reviewer interests form at **www.sgm.ac.uk**. A classified compendium of reviews from 1996 to the present is also available on the website.

What Bugged the Dinosaurs? Insects, Disease, and Death in the Cretaceous

By G. Poinar Jr & R. Poinar
Published by Princeton University Press (2008)
£17.95 pp. 264
ISBN 0-69112-431-5



I was intrigued by dinosaurs as a child. They were so majestic and powerful, part of a fantasy world I could never quite imagine. This book attempts to answer the question of how they became extinct. George and Roberta Poinar propose that microbes played an important role in the demise of the dinosaurs at the end of the Cretaceous. Their evidence centres around three amber deposits made between 135 and 80 million years ago which provide a plethora of fossilized insects that have recently been found to contain pathogenic microbes. The process of fossilization is selective and an incomplete record causes problems. However, the authors explain how the evidence supports their hypothesis.

By comparing insects fossilized in amber to those that exist today, palaeontologists can determine the likelihood of pathogens being present. In an '*intricate case of detective work*', the Poinars first discovered pathogenic microbes in a fossilized sand fly, along with vertebrate blood cells. Today, blood-sucking insects are a major source of disease. The authors suggest that things were not so different in the Cretaceous. Dinosaurs had surprisingly thin scales with small openings, and the spaces between scales offered them even less protection against insects. Even if the skin proved difficult to penetrate, the areas around the mouth, eyes, ears and nose would have been much more accessible.

The amber deposits suggest that biting midges were quite common in the Cretaceous. Morphologically, the fossilized creatures are related to reptile biters, so the authors suggest they may have fed on dinosaurs. They suggest that an allergic reaction to a bite could have led to scratching, which can cause bacterial and fungal infections and could be life-threatening. The amber deposits also provided researchers with evidence of a Cretaceous malarial parasite, *Paleohaemoproteus*, which could have caused a fatal infection in dinosaurs. Black flies carried the malarial parasite *Leucocytozoon* and mosquitoes, horseflies, ticks and fleas may also have transmitted disease. The authors suggest that emerging contagious diseases may have spread among dionsaur populations.

Dinosaurs may also have been affected by microbes indirectly. Plant diseases would have depleted the food supply, potentially causing herbivores to starve. Although initially this would have provided carnivores with easy prey, they too would eventually have starved.

Some of the chapters begin with a description of a fictional (but possible) scenario. Although some of these paint a vivid picture, they can distract the reader from the story and are sometimes difficult to read because they are so packed full of adjectives. Nonetheless, they show the enthusiasm the authors have for the subject, as do the numerous personal anecdotes in the text.

The extinction of the dinosaurs is hotly debated, primarily swinging between two schools of thought: that the extinction happened quickly (catastrophists) versus slowly (gradualists). The arguments are explained well at the end of the book, although some clarification may have been useful earlier in the text.

Readers with little prior knowledge of palaeontology may find some chapters hard-going – continuous references (with no explanations) to types of dinosaurs, time periods and prehistoric trees can stagnate the flow of the narrative. Appendix C is a useful resource for readers not trained in the science, as it shows the problems associated with palaeontological evidence and evaluating the fossil record. Unfortunately, an incoherent order makes an otherwise comprehensive reference list difficult to use.

Insects are central to this book, with a whole chapter dedicated to explaining how they managed to survive when all the dinosaurs died out. In my opinion, the story of the microbes is somewhat neglected and some mistakes creep in. A chapter on insects as sanitary engineers explains how, without insects to decompose excrement and cadavers, the Cretaceous world would have been almost uninhabitable. The authors applaud termites for their good job at keeping things clean, but do not refer to their essential endosymbionts! The important role of microbes as decomposers is also not acknowledged sufficiently.

I would certainly recommend this book to anyone interested in dinosaurs and prehistoric life in general. It has changed the way I imagine the Cretaceous and the extinction of the dinosaurs and I am sure it will open up new avenues of thought in this area.

***Lucy Goodchild**, SGM*

Hobbs' Food Poisoning and Food Hygiene 7th Edition

Edited by J. McLauchlin & C. Little
Published by Hodder Arnold Education (2007)
£19.99 pp. 412
ISBN 0-34090-530-2

This may be a little different from a normal review, but I'll start at the end; whether to recommend the book? Well, I was so struck by the book's layout and design, that within 30 minutes I had added it to our list of recommended texts for our Environmental Health degree courses, and requested our libraries to purchase additional copies!

I already have a number of earlier versions of '*Hobb's*', although I confess that editions 4 to 6 had escaped my notice. I therefore cannot comment on how this version compares with the previous edition. Neverthess, the layout of this version is first thing which strikes you; the use of colour for headings in the text, tables and figures, and the use of colour photos. This makes the book pleasing to browse through, and captivates your attention. Some notable pictures are those of the microbial flora of hands after handling cloths, etc.; super for getting the message across.

It is a multiauthored book, with many of the writers from the UK Health Protection Agency (HPA), and Food Standards Agency. Therefore, the information is authoritative, and advantage has been taken to frequently include data from the HPA in the figures and tables. Part 1 covers the role of microbiology in food poisoning and food-borne infections. Part 2 is concerned with food hygiene in the prevention of food poisoning. The final part is divided into chapters on the contribution of food poisoning and hygiene in specific settings.

The first section covers the core aspects, in 7 chapters, and introduces the reader to major food-borne pathogens, their sources and diversity. Infections, intoxications and prions are covered. The chapter on parameters controlling bacterial growth includes preservation as well as food spoilage. The chapter on epidemiology includes interesting, well-illustrated examples of outbreaks. The final chapter is on water-borne disease and sewage/sludge disposal. As already stated, since many of the authors are from government agencies, the reader benefits from the inclusion of information on policy development, standards and legislation.

The second part has 12 chapters focussed on food hygiene. The opening chapter is on personal hygiene of the food handler, and the chapter's progress to food preparation, manufacture, the retail trade. Cleaning and disinfection, and pest control are dealt with in separate chapters. Whereas the majority of the book is UK-orientated, there is one chapter on food hygiene in developing countries, and another on food hygiene in the wilderness.

The third, and final part, gives the reader an interesting insight into the relevance of food poisoning and hygiene in various sector groups. The areas range from healthcare, ships, aircraft, seaports, as well as the environmental health, medical and veterinary practitioners.

Christine Little and Jim McLauchin should be congratulated on such a well constructed text on the broad subjects that are encompassed in the subject of food poisoning. Inevitably, with such a range of topics and authors, there is likely to be some overlap, as occurs with the topic of food poisoning outbreaks in chapters 6 and 32. But this is a minor issue for a book which can give so much concise information, in such a well-designed format to aid effective learning. I can well imagine professional hygiene trainers delving into this book time and time again.

While I was very enthusiastic to include the book for our Environmental Health students, whether to use it as a core text on a food microbiology degree course is less strong. Nevertheless, I would certainly recommend it as a supporting text, and essential background reading. The reason for this is that the chapters are light on reference material in some chapters, and the UK focus. This is a two-edged sword, since the UK emphasis is of great benefit to environmental health students; however, it is of less international relevance. At the end of the day, the cover price of £19.99 makes this a formidable information per pound book; it is definitely going to be well-thumbed for my lecture presentations.

***Stephen Forsythe**, Nottingham Trent University*

Reviews on the web

Reviews of the following books are available on the website at www.sgm.ac.uk/pubs/micro_today/reviews.cfm

Environmental Genomics
Legionella *Molecular Microbiology*
Microcosm: E. coli *and The New Science of Life*
MicroRNAs From Basic Science to Disease Biology
Chemical Communication among Bacteria
High-Pressure Microbiology
Food-Borne Viruses: Progress and Challenges
Structural Proteomics: High-Throughput Methods
Food-borne Diseases
Avian Influenza Virus
Microbial Ecology of Aerial Plant Surfaces
Viral Therapy of Cancer
Campylobacter, *3rd edn*
Referenced Review Questions in Pharmacogenomics
Paramecium *Genetics and Epigenetics*
Fundamentals of Biofilm Research

comment

Scotoma in contemporary microbiology

Howard Gest explodes what he considers to be the myth of 'unculturable' bacteria.

The eminent neurologist Dr Oliver Sacks describes scotoma as involving the deletion of what was originally perceived, a loss of knowledge, a loss of insight … a regression to less perceptive explanations. '*All these not only beset neurology but are surprisingly common in all fields of science. They raise the deepest questions about why such lapses occur.*' A scotoma has apparently afflicted many molecular biologists, and others, who maintain that most (>95 %) of bacteria living in nature are 'unculturable' in the laboratory. This view is frequently used as a crutch to justify molecular metagenomics as the panacea for understanding the complexities of bacterial ecology.

The myth of unculturability is repeated so often that it has penetrated to semi-popular science writing. In a recent issue of the *American Scientist*, Dorit asks '*Why did it take so long to acknowledge our inner microbe? The answer stems, in part, from the fact that most bacteria cannot be grown in the laboratory. Consequently, until recently, microbiologists could not identify – let alone understand – microbes that refused to live in the world of Petri dishes and culture flasks.*'

The myth of 'unculturability' persists because it is promoted by scientists who have little experience in growing fastidious bacteria or knowledge of past investigations in which nutritional idiosyncracies of numerous types of organisms were defined by intensive studies. For over a century, a legion of microbiologists has provided numerous examples of bacteria that have complex growth requirements that are not satisfied by simple concoctions of yeast extract and similar supplements. An interesting case in point: in 1910, F.W. Twort undertook to isolate the agent responsible for tuberculosis of cattle. The disease was causing great losses of cattle in Britain and Europe. In a classic 1911 paper, Twort and his colleague Ingram noted, '*All writers on this disease state that the causative agent cannot be cultivated outside the animal body*'. They went on to demonstrate that *Mycobacterium pseudotuberculosis* can be grown in pure culture by adding extracts of dead cells of *Mycobacterium phlei*. This was one of the earliest researches showing requirements of many bacteria for 'essential' growth factors, later identified in this instance to be a form of vitamin K.

In support of the myth of unculturability, it is repeatedly claimed that '*only a fraction of less than 1 % of bacteria on or in natural sources can be recovered as colonies on standard laboratory media.*' This, of course, is a vague and inadequate criterion of culturability. As indicated by Twort & Ingram, it is not news to knowledgeable microbiologists that the definition of nutritional requirements of bacteria is often difficult and requires lengthy laboratory studies. To illustrate the point, I have posted several more significant examples from the literature on the web at http://hdl.handle.net/2022/3149

My critique of the myth of 'unculturability' on the internet is '*dedicated to the pioneering microbiologists who isolated pure cultures of microbes responsible for (a) infectious diseases of animals and plants, and (b) the cyclic transformations of major chemical elements on the Earth. Their characterization of the biological, physiological, and genetic properties of these organisms paved the way for current research.*' The careers and contributions of more than 300 of the early pioneers are profiled in William Bulloch's 1938 classic book *The History of Bacteriology*. Back in 1993, I summarized the problem under discussion as follows: '*The requirements for growth and reproduction of extant species of bacteria are obviously met in environments that provide appropriate chemical and physical conditions. Whether or not the requirements can be satisfied in the laboratory depends on many factors, which include the knowledge, skill, and patience of the investigator … There is no doubt that studies on nucleic acid sequences of bacterial species are enlarging our understanding of species relationships and evolutionary patterns. But justification for pursuing such research hardly needs to be based on the myth that the 'molecular approach' is necessary because many species are 'unculturable'.*'

In my opinion, the study of pure cultures remains the most reliable source of basic information for understanding the properties and evolutionary relationships of the vast majority of bacteria, as well as the dynamics of changes they catalyse in the biosphere.

▲ *Tek Image / Science Photo Library*

Howard Gest
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Further reading

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Twort. F.W. & Ingram, G. (1911). *Proc R Soc* LXXXIV, 517–542.

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